TOXICOLOGICAL PROFILE FOR PLUTONIUM

Agency for Toxic Substances and Disease Registry
U.S. Public Health Service

In collaboration with:

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The use of company name or product name(s) is for identification only and does not imply endorsement by the Agency for Toxic Substances and Disease Registry.

FOREWORD

The Superfund Amendments and Reauthorization Act (SARA) of 1986 (Public Law 99-499) extended and amended the Comprehensive Environmental Response, Compensation, and Liability Act of 1980 (CERCLA or Superfund). This public law directed the Agency for Toxic Substances and Disease Registry (ATSDR) to prepare toxicological profiles for hazardous substances which are most commonly found at facilities on the CERCLA National Priorities List and which pose the most significant potential threat to human health, as determined by ATSDR and the Environmental Protection Agency (EPA). The lists of the 250 most significant hazardous substances were published in the Federal Register on April 17, 1987, on October 20, 1988, on October 26, 1989, and on October 17, 1990.

Section 104(i)(3) of CERCLA, as amended, directs the Administrator of ATSDR to prepare a toxicological profile for each substance on the list. Each profile must include the following content:

(A) An examination, summary, and interpretation of available toxicological information and epidemiological evaluations on the hazardous substance in order to ascertain the levels of significant human exposure for the substance and the associated acute, subacute, and chronic health effects,

(B) A determination of whether adequate information on the health effects of each substance is available or in the process of development to determine levels of exposure which present a significant risk to human health of acute, subacute, and chronic health effects, and

(C) Where appropriate, an identification of toxicological testing needed to identify the types or levels of exposure that may present significant risk of adverse health effects in humans.

This toxicological profile is prepared in accordance with guidelines developed by ATSDR and EPA. The original guidelines were published in the Federal Register on April 17, 1987. Each profile will be revised and republished as necessary, but no less often than every three years, as required by CERCLA, as amended.

The ATSDR toxicological profile is intended to characterize succinctly the toxicological and adverse health effects information for the hazardous substance being described. Each profile identifies and reviews the key literature (that has been peer-reviewed) that describes a hazardous substance's toxicological properties. Other pertinent literature is also presented but described in less detail than the key studies. The profile is not intended to be an exhaustive document; however, more comprehensive sources of specialty information are referenced.

Foreword

Each toxicological profile begins with a public health statement, which describes in nontechnical language a substance's relevant toxicological properties. Following the public health statement is information concerning significant health effects associated with exposure to the substance. The adequacy of information to determine a substance's health effects is described. Data needs that are of significance to protection of public health will be identified by ATSDR, the National Toxicology Program (NTP) of the Public Health Service, and EPA. The focus of the profiles is on health and toxicological information; therefore, we have included this information in the beginning of the document.

The principal audiences for the toxicological profiles are health professionals at the federal, state, and local levels, interested private sector organizations and groups, and members of the public.

This profile reflects our assessment of all relevant toxicological testing and information that has been peer reviewed. It has been reviewed by scientists from ATSDR, the Centers for Disease Control, the NTP, and other federal agencies. It has also been reviewed by a panel of nongovernment peer reviewers and is being made available for public review. Final responsibility for the contents and views expressed in this toxicological profile resides with ATSDR.

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Administrator
Agency for Toxic Substances and
Disease Registry

CONTENTS

LIST OF FIGURES

LIST OF TABLES

1. PUBLIC HEALTH STATEMENT

This Statement was prepared to give you information about plutonium and to emphasize the human health effects that may result from exposure to it. The Environmental Protection Agency (EPA) has identified 1.177 sites on its National Priorities List (NPL). Plutonium has been found above background levels at five of these sites. However, we do not know how many of the 1,177 NPL sites have been evaluated for plutonium. As EPA evaluates more sites, the number of sites at which plutonium is found may change. The information is important for you because plutonium may cause harmful health effects and because these sites are potential or actual sources of human exposure to plutonium.

When a radioactive chemical is released from a large area such as an industrial plant, or from a container such as a drum or bottle, it enters the environment as a radioactive chemical. This emission, which is also called a release, does not always lead to exposure. You can be exposed to a chemical only when you come into contact with the chemical. You may be exposed to it in the environment by breathing, eating, or drinking substances containing the chemical or from skin contact with it.

If you are exposed to a hazardous substance such as plutonium, several factors will determine whether harmful health effects will occur and what the type and severity of those health effects will be. These factors include the dose (how much), the duration (how long), the route or pathway by which you are exposed (breathing, eating, drinking, or skin contact), the other chemicals to which you are exposed, and your individual characteristics such as age, sex, nutritional status, family traits, life style, and state of health.

1.1 WHAT IS PLUTONIUM?

Plutonium is a silvery-white radioactive metal that exists as a solid under normal conditions. It is produced when uranium absorbs an atomic particle. Small amounts of plutonium occur naturally, but large amounts have been produced by man in nuclear reactors. Plutonium can be found in the environment in several forms called isotopes. The most common plutonium isotopes are plutonium-238 and plutonium-239. Because plutonium is a radioactive element, it constantly changes or "decays." In this decay process, energy is released and a new product is formed. The energy released is called radiation. When plutonium decays, it divides into two parts -- a small part that we call "alpha" radiation and the remainder, different from original plutonium, called the daughter. The daughter is also radioactive, and it, too, continues to decay until a nonradioactive daughter is formed. During these decay processes, alpha, beta, and gamma radiation are released. Alpha particles can travel only very short distances and cannot go through the

thickness of your skin. Beta particles can travel farther and can penetrate a few millimeters into your tissues. Gamma radiation travels the farthest and can go all the way through your body. It takes about 90 years for one-half of a quantity of plutonium-238 to break down to its daughter and about 24,000 years for this to happen to plutonium-239.

Plutonium-238 is used to provide on board power for electronic systems in satellites. Plutonium-239 is used primarily in nuclear weapons. Most plutonium is found combined with other substances, for example, plutonium dioxide (plutonium with oxygen) or plutonium nitrate (plutonium with nitrogen and oxygen). More information about the properties and uses of plutonium can be found in Chapters 3, 4, and 5.

1.2 HOW MIGHT I BE EXPOSED TO PLUTONIUM?

Plutonium has been released to the environment primarily by atmospheric testing of nuclear weapons and by accidents at weapons production and utilization facilities. In addition, accidents involving weapons transport, satellite reentry, and nuclear reactors have also released smaller amounts of plutonium into the atmosphere. When plutonium was released to the atmosphere, it returned to the earth's surface as fallout. Average fallout levels in soils in the United States are about 2 millicuries (mCi)/square kilometer (about 0.4 square miles) for plutonium-239 and 0.05 mCi/square kilometer for plutonium-238. A millicurie is a unit used to measure the amount of radioactivity; 1 mCi of plutonium-239 weighs 0.016 gm, while 1 mCi of plutonium-238 weighs 0.00006 gm. Measurements in air have been made at a few locations. For example, air levels of plutonium-239 in New York City in the 1970s were reported to be 0.00003 picocuries (pCi) per cubic meter of air. One pCi is one billionth of a mCi. Persons who work at nuclear plants using plutonium have a greater chance of being exposed than individuals in the general population. However, you could be exposed to plutonium if there was an accidental release of plutonium during use, transport, or disposal. Because plutonium does not release very much gamma radiation, harmful health effects are not likely to occur from being near plutonium unless you breathe or swallow it. You may find more information about exposure to plutonium in Chapter 5.

1.3 HOW CAN PLUTONIUM ENTER AND LEAVE MY BODY?

You are most likely to be exposed to plutonium by breathing it in. Once breathed in, the amount that stays in the lungs depends upon several things, particularly the particle size and form of the plutonium compound breathed in. The forms that dissolve easily may be absorbed (pass through the lungs into other parts of the body) or some may remain in the lung. The forms that dissolve less easily are often coughed up and then swallowed. However, some of these may also remain in the lung. Plutonium taken in with food or water is poorly absorbed from the stomach, so most of it leaves the body in feces. Absorption of

plutonium through undamaged skin is very limited, but it may enter the body through wounds.

Some of the plutonium absorbed into the body leaves the body in urine. The rate of plutonium removal from the tissues of the body is very slow, however, occurring over years. Most of the plutonium that stays in the body is found in the lungs, liver, and sireleton. You may find more information about this subject in Chapter 2.

1.4 HOW CAN PLUTONIUM AFFECT MY HEALTH?

Plutonium may remain in the lungs or move to the bones, liver, or other body organs. It generally stays in the body for decades and continues to expose the surrounding tissues to radiation. This may eventually increase your chance of developing cancer, but it would be several years before such cancer effects became apparent. The experimental evidence is inconclusive, and studies of some human populations who have been exposed to low levels of plutonium have not definitely shown an increase in cancer. However, plutonium has been shown to cause both cancers and other damage in laboratory animals, and might affect the ability to resist disease (immune system). We do not know if plutonium causes birth defects or affects the ability to have children. However, radioactivity from other radioactive compounds can produce these effects. If plutonium can reach these sensitive target tissues, radioactivity from plutonium may produce these effects. More information on the health effects of plutonium is presented in Chapter 2.

1.5 WHAT LEVELS OF EXPOSURE HAVE RESULTED IN HARMFUL HEALTH EFFECTS?

Plutonium is odorless and tasteless so you cannot tell if you are being exposed to plutonium. If you breathe in plutonium, some of it will be retained in your body. When discussing harmful health effects, the amount of plutonium that caused these effects is usually given as the amount of plutonium retained or deposited in the body rather than as the amount that was in the air. As indicated in Tables l-l through 1-4, there is no information from studies in humans or animals to identify the specific levels of exposures to plutonium in air, food, or water that have resulted in harmful effects. However, it is generally assumed that any amount of absorbed radiation, no matter how small, may cause some damage. When expressed as the amount of radioactivity deposited in the body per kilogram of body weight (kg bw) as a result of breathing in plutonium, studies in dogs report that 100,000 pCi plutonium/kg bw caused serious lung damage within a few months, 1,700 pCi/kg bw caused harm to the immune system, and 1,400 pCi/kg bw caused bone cancer after 4 years. In each of these cases the dogs were exposed to the plutonium

TABLE 1-1. Human Health Effects from Breathing Plutonium*

Short-term Exposure (less than or equal to 14 days)		
Levels in Air	Length of Exposure	Description of Effects
		The health effects resulting from short-term exposure of humans breathing specific levels of plutonium are not known.
Long-term Exposure (greater than 14 days)		
Levels in Air	Length of Exposure	Description of Effects
		The health effects resulting from long-term exposure of humans breathing specific levels of plutonium are not known.

*See Section 1.2 for a discussion of exposures encountered in daily life.

TABLE 1-2. Animal Health Effects from Breathing Plutonium

Short-term Exposure (less than or equal to 14 days)		
Levels in Air	Length of Exposure	Description of Effects
		The health effects resulting from short-term exposure of animals breathing specific levels of plutonium are not known.
Long-term Exposure (greater than 14 days)		
Levels in Air	Length of Exposure	Description of Effects
		The health effects resulting from long-term exposure of animals breathing specific levels of plutonium are not known.

TABLE 1-3. Human Health Effects from Eating or Drinking Plutonium*

Short-term Exposure (less than or equal to 14 days)		
Levels in Food	Length of Exposure	Description of Effects
		The health effects resulting from short-term exposure of humans to food containing specific levels of plutonium are not known.
Levels in Water		
		The health effects resulting from short-term exposure of humans to water containing specific levels of plutonium are not known.
Long-term Exposure (greater than 14 days)		
Levels in Food	Length of Exposure	Description of Effects
		The health effects resulting from long-term exposure of humans to food containing specific levels of plutonium are not known.
Levels in Water		
		The health effects resulting from long-term exposure of humans to water containing specific levels of plutonium are not known.

*See Section 1.2 for a discussion of exposures encountered in daily life.

TABLE 1-4. Animal Health Effects from Eating or Drinking Plutonium

Short-term Exposure (less than or equal to 14 days)		
Levels in Food	Length of Exposure	Description of Effects
		The health effects resulting from short-term exposure of animals to food containing specific levels of plutonium are not known.
Levels in Water		The health effects resulting from short-term exposure of animals to water containing specific levels of plutonium are not known.
Long-term Exposure (greater than 14 days)		
Levels in Food	Length of Exposure	Description of Effects
		The health effects resulting from long-term exposure of animals to food containing specific levels of plutonium are not known.
Levels in Water		The health effects resulting from long-term exposure of animals to water containing specific levels of plutonium are not known.

in air for one day. You can find more information on the health effects of plutonium in Chapter 2.

1.6 IS THERE A MEDICAL TEST TO DETERMINE WHETHER I RAVE BEEN EXPOSED TO PLUTONIUM?

There are tests available that can reliably measure the amount of plutonium in a urine sample even at very low levels. These measurements can be used to estimate the total amount of plutonium that is carried by the body. However, these measurements cannot be used to directly determine the levels to which the person was exposed or to predict the potential for health effects. In addition, there are tests to measure plutonium in soft tissues (such as body organs), feces, bones, and milk. These tests are not routinely available in your doctor's office because special laboratory equipment is required. You can find more information on methods used to measure levels of plutonium in Chapters 2 and 6.

1.7 WHAT RECOMMENDATIONS HAS THE FEDERAL GOVERNMENT MADE TO PROTECT HUMAN HEALTH?

Guidelines for radiation protection have been established for the general public and for occupational settings. These guidelines are expressed in units called rems. A rem is a unit that measures the amount of radiation absorbed by the body. For people in the general population, national guidelines recommend dose limits of 0.5 rems/year, while international guidelines set dose limits of 0.5 rems/year for short-term exposure and 0.1 rems/year for long-term exposure. For workers in industries where exposure to radiation may occur, the EPA has recommended a dose limit of 5 rems/year. This is the same dose limit set for workers by the International Commission on Radiological Protection (ICRP). The ICRP has developed limits for the amount of radioactivity we take into the body, called Annual Limits on Intake (ALIs), and for the amount of radioactivity in the air we breathe, called Derived Air Concentrations (DACS). For workers exposed to plutonium-239 in air, the AL1 is 20,000 pCi/year and the DAC is 7 pCi/m^3 of air. The ALIs and DACs vary with each plutonium isotope. You may find more information on regulations and guidelines in Chapter 7.

1.8 WHERE CAN I GET MORE INFORMATION?

If you have any more questions or concerns not covered here, please contact your State Health or Environmental Department or:

Agency for Toxic Substances and Disease Registry
Division of Toxicology
1600 Clifton Road, E-29
Atlanta, Georgia 30333

This agency can also give you information on the location of the nearest occupational and environmental health clinics. Such clinics specialize in recognizing, evaluating, and treating illnesses that result from exposure to hazardous substances.

2. HEALTH EFFECTS

2.1 INTRODUCTION

This chapter contains descriptions and evaluations of studies and interpretation of data on the health effects associated with exposure to plutonium. Its purpose is to present levels of significant exposure to plutonium based on toxicological studies, epidemiological investigations, and environmental exposure data. This information is presented to provide public health officials, physicians, toxicologists, and other interested individuals and groups with (1) an overall perspective of the toxicology of plutonium and (2) a depiction of significant exposure levels associated with various adverse health effects.

Plutonium is a radioactive element. Radioactive elements are those that undergo spontaneous transformation (decay) in which energy is released (emitted) either in the form of particles, such as alpha or beta particles, or waves, such as gamma or X-ray. This transformation or decay results in the formation of new elements, some of which may themselves be radioactive, in which case they will also decay. The process continues until a stable (nonradioactive) state is reached (see Appendix B for more information).

Radionuclides can produce adverse health effects as a result of their radioactive properties. With toxicity induced by the chemical properties of an element or its compounds, the adverse effects are characteristic of that specific substance. With toxicity induced by radioactive properties, the adverse effects are independent of the chemical toxicity and are related to the amount and type of radiation absorbed by the target tissues or organs. While the chemical properties affect the distribution and biological half-life of a radionuclide and influence the retention of the radionuclide within a target organ, the damage from a type of radiation is independent of the source of that radiation. The adverse health effects reported in Chapter 2 are related to the radioactive properties of plutonium rather than its chemical properties. In this profile, there is little or no specific information regarding the influence of plutonium on specific target organs in humans, leading to reproductive, developmental, or carcinogenic effects. There is evidence, however, from the large body of literature concerning radioactive substances that alpha radiation can affect these processes in humans (BEIR IV 1988; UNSCEAR 1982) (see Appendix B for additional information on the biological effects of radiation).

Plutonium exists in several isomeric forms, the most important of which are plutonium-238 and plutonium-239. When plutonium decays, it emits primarily alpha particles (ionized helium atoms), except for plutonium-241 which decays by beta emission. Alpha particles are highly ionizing and, therefore, damaging, but their penetration into tissue is

slight. Biological damage is limited to cells in the immediate vicinity of the alpha-emitting radioactive material.

The potential for adverse health effects caused by the plutonium isotopes is dependent on several factors including solubility, distribution in the various body organs, the biological retention time in tissue, the energy of the radioactive emission, and the half-life of the isotope (EPA 1977). A potential health hazard results when plutonium is inhaled and deposited in lung tissue or is ingested or enters the body through wounds. Subsequent translocation of some of the plutonium from the lungs to tissues and organs distant from the site of entry results in radiation damage to these tissues as well as to the lung. For the two most studied isotopes, plutonium-238 and plutonium-239, radioactive half-life (86 and 24,000 years, respectively) and biological retention time are very long, resulting in prolonged exposure of body organs to alpha radiation (EPA 1977). Plutonium isotopes generally exist as complexes with other elements or compounds (see Chapter 3 for information on chemical and physical properties of plutonium and plutonium compounds). Plutonium-238 compounds and certain plutonium-239 compounds, such as the nitrate forms, are more soluble in lung tissue than plutonium-239 dioxide. Thus, plutonium-239 dioxide will be retained longer in lung tissue following inhalation than the more soluble forms, plutonium-238 compounds or plutonium-239 nitrate. Insoluble plutonium is inhaled as particles. Particle size determines deposition patterns and consequently, clearance patterns from the lung; therefore, particle size is directly related to retention and the resulting radiological dose. These characteristics also affect the toxicity and target organs of the various isotopes.

Numerous studies have been conducted in laboratory animals to develop a better understanding of the physiological effects of exposure to plutonium. These studies have increased our understanding of the deposition of plutonium in various body organs and of the time of retention, as well as providing an extensive database on the adverse health effects of plutonium. The relevant toxicological properties of plutonium and significant health effects related to exposure to plutonium are described in this chapter.

2.2 DISCUSSION OF HEALTH EFFECTS BY ROUTE OF EXPOSURE

To help public health professionals address the needs of persons living or working near hazardous waste sites, the data in this section are organized first by route of exposure -- inhalation, oral, and dermal -- and then by health effect -- death, systemic, immunological, neurological, developmental, reproductive, genotoxic, and carcinogenic effects. These data are discussed in terms of three exposure periods -- acute, intermediate, and chronic.

2. HEALTH EFFECTS

Levels of significant exposure for each exposure route and duration (for which data exist) are presented in tables and illustrated in figures. The points in the figures showing no-observed-adverse-effect levels (NOAELS) or lowest-observed-adverse-effect levels (LOAELs) reflect the actual levels of exposure used in the studies. LOAELs have been classified into "less serious" or "serious" effects. These distinctions are intended to help the users of the document identify the levels of exposure at which adverse health effects start to appear, determine whether or not the intensity of the effects varies with dose and/or duration, and place into perspective the possible significance of these effects to human health.

The significance of the exposure levels shown in the tables and figures may differ depending on the user's perspective. For example, physicians concerned with the interpretation of clinical findings in exposed persons or with the identification of persons with the potential to develop such disease may be interested in levels of exposure associated with “serious” effects. Public health officials and project managers concerned with response actions at Superfund sites may want information on levels of exposure associated with more subtle effects in humans or animals (LOAEL) or exposure levels below which no adverse effects (NOAEL) have been observed. Estimates of levels posing minimal risk to humans (Minimal Risk Levels, MRLs) are of interest to health professionals and citizens alike.

The activity of radioactive elements has traditionally been specified in curies (Ci). The curie is approximately 37 billion disintegrations (decay events) per second ($3.7x10x^{10}$ dps). In discussing plutonium, a smaller unit, the picocurie (pCi) is used, where 1 pCi is equal to $1x10^{-12}$ Ci. In international usage, the S.I. unit (the International System of Units) for activity is the Becquerel (Bq), which is equal to one disintegration per second or about 27 pCi. (Information for conversion between units is given in Chapter 9 and Appendix B.) In the text of this profile units expressed in pCi are followed by units in Bq contained in parentheses. The activity concentration is a description of the amount of plutonium deposited in lungs after inhalation exposure or administered to animals by the oral route or by other routes of exposure rather than an expression of dose. In radiation biology, the term dose refers specifically to the amount of energy imparted by the emitted radiation that is absorbed by a particular tissue or organ. This dose is expressed in rads (Grays).

2.2.1 Inhalation Exposure

Numerous inhalation studies in rats, mice, hamsters, dogs, and nonhuman primates have been, conducted or are still on-going. In the majority of these studies, the test animals received a single inhalation exposure to either plutonium-238 or plutonium-239, administered as the dioxide, the citrate, or the nitrate. Observation continued, or is

continuing, for the lifespan of the animals. Among the issues studied were the comparative toxicity of plutonium-238 and plutonium-239, the effect of particle size on deposition and expressed toxicity, the effect of age at first exposure, the target organs and time-course of the disease process, and the differences in species sensitivity. In each case, animals were exposed by inhalation to an aerosol of plutonium particles of different aerodynamic sizes and to different amounts of radioactivity in the aerosol. Environmental levels (i.e., the amount of plutonium radioactivity present in the aerosol) were usually not given. Rather, the amount of plutonium was expressed as a "lung burden" or "initial alveolar deposition" or "initial lung deposition," i.e., the total amount of radioactivity retained in the lung after the exposure. Working from experiment-specific body weights, plutonium deposition levels in this profile have been expressed as pCi plutonium/kg body weight. When literature values were expressed as "radioactivity per gram of lung tissue," these values were also converted to pCi plutonium/kg body weight if lung weight or ratio of lung weight to body weight was given. Health effects associated with plutonium deposition, in units of pCi plutonium/kg body weight, for acute, intermediate, and chronic exposure duration (for which data exist) are presented in Table 2-l and illustrated in Figure 2-l.

2.2.1.1 Death

Analyses of mortality among persons chronically exposed to plutonium in the workplace have been conducted. In the three occupational cohorts studied (Los Alamos Laboratory, Rocky Flats facility, and Hanford Plant), there were consistently fewer deaths than expected based on data for United States white males (Gilbert and Marks 1979; Voelz et al. 1983a, 1983b; Wilkinson et al. 1987). This phenomenon is generally attributed to the "healthy worker effect," which holds that individuals in the work force are healthier than those in the general population. However, in a refined cohort from the Rocky Flats facility, the mortality of plutonium-exposed workers was compared to that of unexposed workers from the same plant. It was reported that death from all causes was elevated in exposed individuals but the increase was not statistically significant (Wilkinson et al. 1987).

Statistically significant decreases in mean survival time in treated animals compared to controls have been reported in rats, mice, hamsters, dogs, and baboons following a single, acute inhalation exposure to plutonium-239 or plutonium-238. A single exposure to plutonium-239 resulting in deposition levels ranging from $2.3x10^{4}$ to $7.2x10^{6}$ pCi ($8.5x10^{2}$ to $2.7x10^{5}$ Bq)/kg body weight produced a decrease in survival time in rats (Metivier et al. 1986; Sanders et al. 1976, 1988), in mice (Lundgren et al. 1987), in hamsters (in the high-dose group, males only) (Sanders 1977), in dogs (Dagle et al. 1988; Muggenburg et al. 1987a; Park et al. 1988), and in baboons (Metivier et

TABLE 2-1. Health Effects Associated with Plutonium Deposition - Inhalation

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (pCi/kg)	LOAEL (Effect) Less Serious (pCi/kg)	LOAEL (Effect) Serious (pCi/kg)	Reference	Chemical Species
ACUTE EXPOSURE								
Death								
1	Rat	1d		1.7×10^4		4.9×10^5 (dec lifespan)	Metivier et al. 1986	$^{239}PuO_2$
2	Rat	1d 30 min				2.5×10^6 (dec lifespan)	Sanders et al. 1977	$^{238}PuO_2$
3	Mouse	1d				2.1×10^6 (dec lifespan)	Lundgren et al. 1987	$^{239}PuO_2$
4	Hamster	1d 30 min				2.1×10^4 (dec lifespan)	Sanders 1977	$^{239}PuO_2$
5	Dog	1d				6.2×10^3 (dec lifespan)	Park et al. 1988	$^{239}PuO_2$
6	Dog	1d				2.8×10^4 (dec lifespan)	Park et al. 1988	$^{238}PuO_2$
Systemic								
7	Rat	1d 30 min	Resp			1.6×10^6 (pneumonitis)	Sanders and Mahaffey 1979	$^{239}PuO_2$
8	Rat	1d	Resp			1.6×10^5 (fibrosis)	Sanders et al. 1988	$^{239}PuO_2$
9	Rat	1d 30 min	Resp Other	2.5×10^6		6.3×10^5 (pneumonitis)	Sanders et al. 1977	$^{238}PuO_2$
10	Rat	1d	Resp		4.3×10^5 (inc collagen ct)		Metivier et al. 1978a	$^{239}PuO_2$
11	Mouse	1d (days)	Resp Other	3.6×10^3	8.4×10^5 (biochem effects) 8.4×10^5 (inc lung wt)		Talbot and Moores 1985	$^{239}PuO_2$
12	Hamster	1dose 30 min	Resp Other	1.4×10^6		1.4×10^6 (metaplasia)	Sanders 1977	$^{238}PuO_2$

TABLE 2-1 (continued)

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (pCi/kg)	LOAEL (Effect) Less Serious (pCi/kg)	LOAEL (Effect) Serious (pCi/kg)	Reference	Chemical Species
13	Hamster	1d 30 min	Resp Other	$1.4x10^6$		$1.4x10^6$ (pneumonitis)	Sanders 1977	$^{239}PuO_2$
14	Dog	1d	Resp			$1.0x10^5$ (pneumonitis)	Muggenburg et al. 1987a	$^{239}PuO_2$
15	Dog	1d	Resp Hemato Hepatic		$1.3x10^5$ (lymphopenia) $4.4x10^5$ (altered enz)	$1.3x10^5$ (pneumonitis)	Dagle et al. 1988	$^{239}Pu(NO_3)_4$
16	Dog	1d	Hemato Hepatic		$6.1x10^3$ (lymphopenia) $6.1x10^3$ (inc enzymes)		Park et al. 1988	$^{238}PuO_2$
17	Dog	1d	Resp Hemato Hepatic	$4.6x10^5$	$6.1x10^3$ (dec lymphocytes)	$4.6x10^5$ (pneumonitis)	Park et al. 1988	$^{239}PuO_2$
18	Dog	1d	Resp		$1.1x10^8$ (dec resp funct)		Muggenburg et al. 1988	$^{239}PuO_2$
19	Dog	1d				$1.0x10^6$ (fibrosis)	Mewhinney et al. 1987a	$^{238}PuO_2$
Immunological								
20	Mouse	1d			$4.5x10^4$ (dec macrophage)		Moores et al. 1986	$^{239}PuO_2$
21	Hamster	1d			$7.1x10^4$ (dec Ab form cell)		Bice et al. 1979	$^{239}PuO_2$
22	Dog	1d				$1.7x10^3$ (lymphadenopathy)	Park et al. 1988	$^{239}PuO_2$
23	Dog	1d				$6.1x10^3$ (lymphadenopathy)	Park et al. 1988	$^{238}PuO_2$

TABLE 2-1 (continued)

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (pCi/kg)	LOAEL (Effect) Less Serious (pCi/kg)	LOAEL (Effect) Serious (pCi/kg)	Reference	Chemical Species
Cancer								
24	Rat	1d 30 min				$3.1x10^4$ (CEL-lung)	Sanders et al. 1977	$^{238}PuO_2$
25	Rat	1d				$4.3x10^4$ (CEL-lung)	Sanders et al. 1988	$^{239}PuO_2$
26	Rat	1d				$1.7x10^4$ (CEL-lung)	Metivier et al. 1986	$^{239}PuO_2$
27	Dog	1d				$2.3x10^4$ (CEL-skeletal)	Dagle et al. 1988	$^{239}Pu(NO_3)_4$
28	Dog	1d				$1.4x10^3$ (CEL-skeletal)	Park et al. 1988	$^{238}PuO_2$
29	Dog	1d				$2.1x10^4$ (CEL-lung)	Muggenburg et al. 1987a	$^{239}PuO_2$
30	Dog	1d				$1.9x10^4$ (CEL-liver)	Gillett et al. 1988	$^{238}PuO_2$
31	Dog	1d				$8.7x10^4$ (CEL-lung)	Park et al. 1988	$^{239}PuO_2$
INTERMEDIATE EXPOSURE								
Death								
32	Mouse	1 yr bimonthly				$4.1x10^5$ (dec lifespan)	Lundgren et al. 1987	$^{239}PuO_2$
33	Hamster	1yr bimonthly		$7.1x10^4$			Lundgren et al. 1983	$^{239}PuO_2$

TABLE 2-1 (continued)

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (pCi/kg)	LOAEL (Effect) Less Serious (pCi/kg)	LOAEL (Effect) Serious (pCi/kg)	Reference	Chemical Species
Systemic								
34	Hamster	1 yr bimonthly	Resp			$1.4x10^4$ (pneumonitis)	Lundgren et al. 1983	$^{239}PuO_2$
Cancer								
35	Rat	Multiple				$8.6x10^4$ (CEL-lung)	Sanders and Mahaffey 1981	$^{239}PuO_2$
36	Mouse	1 yr bimonthly				$1.8x10^4$ (CEL-lung)	Lundgren et al. 1987	$^{239}PuO_2$

Ab form cell = antibody forming cells; biochem = biochemical; CEL = cancer effect level; ct = count; d = day; dec = decreased; enz = enzymes; funct = function; Hemato = hematological; inc = increased; LOAEL = lowest observed adverse effect level; min = minute; NOAEL = no observed adverse effect level; Resp = respiratory; wt = weight; yr=year

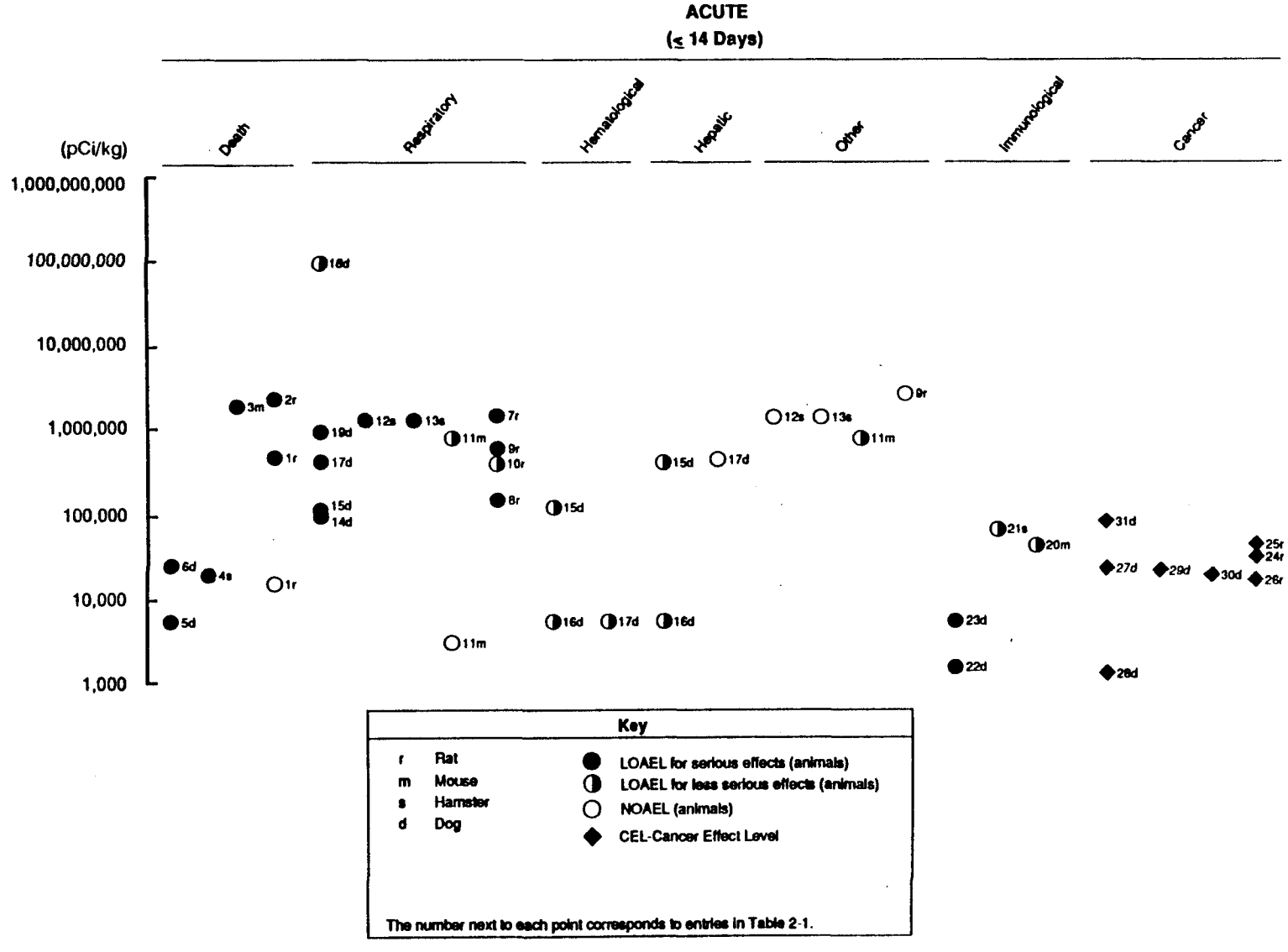

FIGURE 2-1. Health Effects Associated with Plutonium Deposition - Inhalation

80o113-1

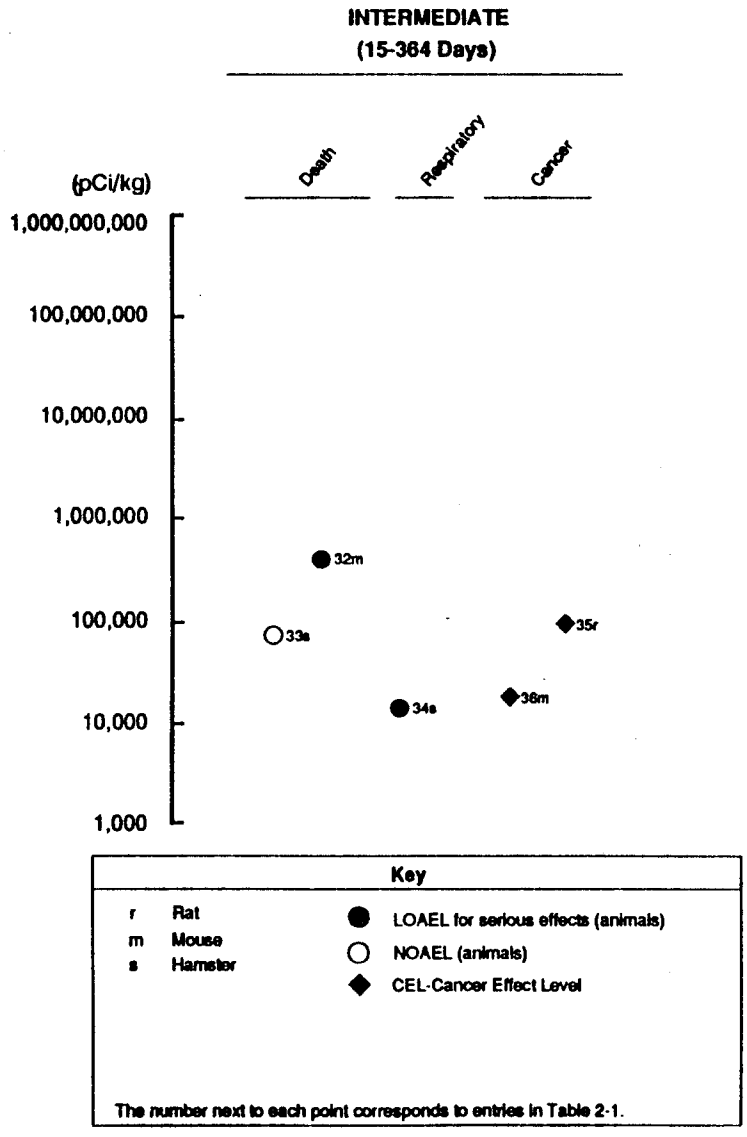

FIGURE 2-1 (Continued)

al. 1974). In all species tested, death occurred within 1 to 3 years after exposure and was usually caused by radiation pneumonitis accompanied by edema, fibrosis, and other signs of respiratory damage. Survival time decreased in a dose-related manner at deposited levels in excess of approximately $1x10^4$ pCi ($3.7x10^2$ Bq) plutonium-239 dioxide/kg body weight.

Similar results were observed in animals given a single, acute inhalation exposure to plutonium-238, as the more soluble dioxide or nitrate (Mewhinney et al. 1987a; Park et al. 1988; Sanders 1977; Sanders et al. 1977). Studies in dogs (Park et al. 1988) and hamsters (Sanders 1977) have demonstrated that plutonium-239 was more toxic than plutonium-238. The primary cause of death in animals treated with plutonium-238 was also radiation pneumonitis.

Exposure of hamsters for an intermediate duration (once every other month for a total of seven doses over 12 months) to plutonium-239 dioxide resulted in a statistically significant decrease in median survival time only in the highest exposure group [at deposition levels of $3.5x10^5$ pCi ($1.3x10^4$ Bq) plutonium-239/kg body weight] (Lundgren et al. 1983). Hamsters receiving lower exposures [at deposition levels of $1.4x10^4$ or $7.1x10^4$ pCi ($5.2x10^2$ or $2.6x10^3$ Bq) plutonium-239/kg body weight] had survival times comparable to controls. Similar exposure of mice (once every other month for a total of six doses over 10 months) to plutonium-239 [at deposited levels of 1.8x104, 8.1x104, or $4.1x10^5$ pCi ($6.7x10^2$, $3.0x10^3$, or $1.5x10^4$ Bq) plutonium-239/kg body weight] resulted in statistically significant decreases in survival in all three exposure groups (Lundgren et al. 1987).

2.2.1.2 Systemic Effects

No studies were located regarding gastrointestinal, cardiovascular, renal, or dermal/ocular effects in humans or animals after inhalation exposure to plutonium.

Respiratory Effects. No studies were located concerning respiratory effects in humans after inhalation exposure to plutonium.

Radiation pneumonitis, characterized by alveolar edema, fibrosis, and, in some cases, pulmonary hyperplasia and metaplasia, has been observed in dogs, mice, rats, hamsters, and baboons following exposure to high levels of plutonium-239 or piutonium-238 dioxide. In dogs, radiation pneumonitis and pulmonary fibrosis were two of the primary causes of death among high-dose groups receiving a lung deposition of approximately $1.0x10^6$ pCi ($3.7x10^4$Bq) plutonium-238/kg body weight (Mewhinney et al. 1987a) or $1.0x10^5$ to $4.6x10^5$ pCi ($3.7x10^3$ to $1.7x10^4$ Bq) plutonium-239/kg body weight (Muggenburg et al. 1987a; Park et al. 1988). The time to death was inversely related to the initial lung

burden; dogs that received approximately 1.0×10^6 pCi (3.7×10^4 Bq) plutonium-238/kg body weight were dead by 600 days post-exposure, while those receiving 2.1×10^5 pCi (7.8×10^3 Bq) plutonium-238/kg body weight survived 1,000 to 2,000 days (Mewhinney et al. 1987a). In dogs. neither the size of the particles (Muggenburg et al. 1987a) nor the age of the animal at initiation of treatment (Guilmette et al. 1987; Muggenburg et al. 1987b) altered the course of the respiratory effects. The pattern of disease in dogs 8 to 10 years old (Muggenburg et al. 1987b) and immature dogs (Guilmette et al. 1987) was similar to that seen in young adult dogs, that is, radiation pneumonitis occurred in the high-exposure groups resulting in shortened survival times. Lung carcinomas were observed in lower exposure groups in which dogs survived for a longer period of time (see Section 2.2.1.8 Cancer and Table 2-l).

Rats also developed radiation pneumonitis within 12 months after a single exposure that resulted in a deposited level of approximately 1.6×10^6 pCi (5.9×10^4 Bq) plutonium-239/kg body weight (Sanders and Mahaffey 1979). However, in another study, temporarily increased collagen deposition, but not pneumonitis, occurred in rats following deposition of 2.810^3 to 2.7×10^6 pCi (1.0×10^2 to 1.0×10^5 Bq) plutonium-239/kg body weight (Metivier et al. 1978a). Radiation pneumonitis and fibrosis were the major pathological findings and causes of death in male hamsters at deposited levels of 1.4×10^5 pCi (5.2×10^4 Bq) plutonium-239/kg body weight (Sanders 1977) or 1.7×10^6 pCi (6.3×10^4 Bq) plutonium-238/kg body weight (Mewhinney et al. 1986).

Baboons and monkeys displayed a respiratory disease pattern similar to that seen in dogs and rodents. Some baboons died of radiation pneumonitis accompanied by pulmonary edema within 50 days after a single exposure to plutonium-239 dioxide at deposited levels of 2.88×10^5 to 7.2×10^6 pCi (1.1×10^4 to 2.7×10^5 Bq)/kg body weight (Metivier at al. 1974; 1978b). Radiation pneumonitis and pulmonary fibrosis were also seen in Rhesus monkeys exposed to plutonium dioxide at deposited levels of 3.4×10^4 to 2.3×10^5 pCi (1.3×10^3 to 8.5×10^3 Bq)/kg body weight (Hahn et al. 1984; LaBauve et al. 1980). Death from pulmonary fibrosis occurred in Rhesus monkeys following lung deposition of 3.4×10^4 pCi (1.3×10^3 Bq) plutonium-239 dioxide/kg body weight (Hahn et al. 1984).

At levels below those that caused acute radiation pneumonitis, chronic alpha irradiation of lung tissue from the deposited plutonium produced interstitial fibrosis. The terminal stage of pneumonitis/fibrosis was characterized by an increased respiratory rate and decreased pulmonary compliance. The cardiopulmonary function of some of the dogs in the study by Muggenburg et al. (1986) was studied further (Muggenburg et al. 1988). Pulmonary dysfunction was observed in these animals and appeared to be a chronic form of radiation pneumonitis or pulmonary fibrosis. The authors noted that this chronic lung injury occurred at lower doses or after a long latency period and, unlike the radiation pneumonitis that was fatal to dogs usually within l-2 years,

occurred over the same time period and same doses as the pulmonary carcinoma.

Exposure of hamsters to plutonium-239 dioxide [at tissue deposition levels of $1.4x10^4$, $7.1x10^4$, or $3.5x10^5$ pCi ($5.2x10^2$, $2.6x10^3$, or $1.3x10^4$ Bq) plutonium-239/kg body weight, once every other month for a total of seven doses over 12 months] resulted in several respiratory effects over lifetime observation (Lundgren et al. 1983). Radiation pneumonitis was observed at all dose levels. Bronchiolar hyperplasia was seen in all groups, including controls, but incidences were statistically significantly increased over controls only in the highest dose group. The highest dose group also showed a statistically significant increase in alveolar squamous metaplasia (Lundgren et al. 1983).

In a similar experiment, mice were exposed (once every other month for a total of six doses over 10 months) to plutonium-239 dioxide resulting in deposition levels ranging from $1.8x10^4$ to $4.1x10^5$ pCi ($6.7x10^2$ to $1.5x10^4$ Bq) plutonium-239/kg body weight, and were observed for life (Lundgren et al. 1987). Radiation pneumonitis and fibrosis were seen only in the highest dose group. However, the incidence of bronchial hyperplasia was statistically significant in the mid- and high-dose groups [at deposition levels of $8.1x10^4$ or $4.1x10^5$ pCi ($3.0x10^3$ or $1.5x10^4$ Bq) plutonium-239/kg body weight]. The highest NOAEL values and all reliable LOAEL values for respiratory effects in each species and duration category are recorded in Table 2-l and plotted in Figure 2-l.

Hematological Effects. No studies were located regarding hematological effects in humans after inhalation exposure to plutonium.

In on-going studies in dogs (Dagle et al. 1988; Park et al. 1988; Ragan et al. 1986) the earliest observed biological effect was in the hematopoietic system. Aerosols of plutonium-239 or plutonium-238, as the dioxide (Park et al. 1988), or plutonium-239 nitrate (Dagle et al. 1988) were each administered at six treatment levels. With plutonium-239 or plutonium-238, as the dioxide, lymphopenia occurred in the four highest exposure groups [at deposited levels of approximately $6.1x10^3$ to $4.6x10^5$ pCi ($2.3x10^2$ to $1.7x10^4$ Bq) plutonium/kg body weight] (Park et al. 1988), but only in the two highest dose groups with plutonium-239 nitrate [$1.3x10^5$-to $4.3x10^5$ pCi ($4.8x10^3$ to $1.6x10^4$ Bq) plutonium-239 nitrate/kg body weight] (Ragan et al. 1986). The lymphopenia was doserelated and correlated both in magnitude and time of appearance postexposure with the initial lung burden for each plutonium isotope. The highest NOAEL values and all reliable LOAEL values for hematological effects in each species and duration category are recorded in Table 2-l and plotted in Figure 2-l.

Hepatic Effects. No studies were located regarding hepatic effects in humans after inhalation exposure to plutonium.

In a study by Dagle et al. (1988), increases in liver enzymes occurred in dogs after a single exposure that resulted in deposition levels above 4.4×10^5 pCi (1.6×10^2 Bq) plutonium-239 nitrate/kg body weight, compared to untreated controls. In dogs, 4 to 13 years following a single inhalation exposure to plutonium-239 dioxide [at deposited lung tissue levels of 2.4×10^4 to 8.7×10^4 pCi (8.9×10^2 to 3.2×10^3 Bq) plutonium-239/kg body weight] the livers were congested, granular, and pigmented (Park et al. 1988).

Exposure of Syrian hamsters to plutonium-239 dioxide (once every other month for a total of seven doses over 12 months) resulted in a statistically significant increase in degenerative liver lesions in tine highest exposure group [at deposition levels of 3.5×10^5 pCi (1.3×10^4 Bq) plutonium-239/kg body weight] (Lundgren et al. 1983). These lesions included degeneration, necrosis, fibrosis, and amyloidosis. However, Lundgren stated that the lesions observed in these hamsters were typical of those usually seen in aged Syrian hamsters. Hamsters receiving lower levels of deposited radioactivity [1.4×10^4 or 7.1×10^4 pCi (5.2×10^2 or 2.6×10^3 Bq) plutonium-239/kg body weight] exhibited nonsignificant increases in liver lesions.

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans after inhalation exposure to plutonium.

Investigations of the radiation effects of plutonium in laboratory animals indicated that translocation of plutonium from the lungs to other tissues was dependent on several factors including the solubility of the plutonium isotope or compound. Translocation to the bone occurred with plutonium citrate and with plutonium nitrate (Bair et al. 1973). By 4,000 days post-exposure, osseous atrophy and radiation osteodystrophy occurred in dogs given a single inhalation exposure to plutonium-238 dioxide (Gillett et al. 1988). The dose which resulted in these specific effects was not reported. For further discussion of this study see Section 2.2.1.8.

2.2.1.3 Immunological Effects

No studies were located regarding the immunological effects in humans after inhalation exposure to plutonium.

Plutonium-239 was transported to the tracheobronchial and mediastinal lymph nodes where it concentrated with time, often reaching higher levels in the lymph nodes than in the lungs (Bair et al. 1973). Lymphadenopathy was associated with a high concentration of plutonium in

the thoracic and hepatic lymph nodes of dogs at lung tissue deposition levels as low as 1.7×10^{3} pCi (6.3×10^{1} Bq) plutonium-239 dioxide/kg body weight or 6.1×10^{3} pCi (2.3×10^{2} Bq) plutonium-238 dioxide/kg body weight (Park et al. 1988). Radiation-related effects in dogs included atrophy and fibrosis of the tracheobronchial lymph nodes (Gillett et al. 1988). Decreases in pulmonary alveolar macrophages in mice (Moores et al. 1986) and depressed-antibody-forming cells in hamsters (Bite et al. 1979) were reported. In addition, decreases in primary antibody responses in dogs (Morris and Winn 1978) were also reported. The highest NOAEL values and all reliable LOAEL values for immunological effects in each species and duration category are recorded in Table 2-1 and plotted in Figure 2-l.

No studies were located regarding the following effects in humans or animals after inhalation exposure to plutonium.

2.2.1.4 Neurological Effects

2.2.1.5 Developmental Effects

2.2.1.6 Reproductive Effects

2.2.1.7 Genotoxic Effects

Epidemiological studies have thus far been limited and have not established conclusively a direct association between plutonium exposure by the inhalation route and increases in genetic effects. A doserelated increase in chromosomal aberrations was observed among 343 plutonium-exposed workers at the Rocky Flats facility. In this group, systemic and lung plutonium burdens of 18.6 to 571.4 pCi (0.69 to 21.2 Bq) plutonium/kg body weight were estimated based on urine analyses and lung deposition estimates (Brandom et al. 1979). Because the frequencies of aberrations were relatively low and the dose estimates imprecise, the authors advised caution regarding use of the data. A study of blood lymphocyte chromosomes of 54 plutonium workers in the United Kingdom was conducted by Tawn et al. (1985). (This study is a continuation of that reported in Schofield (1980).) Systemic body burdens of 114 to >570.8 pCi (4.3 to >21.1 Bq) plutonium/kg body weight were estimated based on urine analyses. While some differences in the distribution of aberrations were seen in the radiation exposed groups, the authors concluded that significant deposits of plutonium did not cause an increase in aberrations. In other studies, Manhattan Project plutonium workers (26 individuals) were followed for 27 to 32 years; no apparent correlation was observed between the frequency of chromosomal aberrations and plutonium body burdens [71.4 to 3.1×10^{3} pCi (2.6 to 114.8 Bq) plutonium/kg body weight based on urine analyses] (Hempelmann et al. 1973; Voelz et al. 1979).

Chromosomal aberrations were observed in Rhesus monkeys and Chinese hamsters following inhalation exposure to plutonium. Increases in

hromosomal aberrations in blood lymphocytes were seen in immature Rhesus monkeys in the high-exposure groups exposed for a single day to plutonium-239 dioxide [deposited levels of $5x10^4$ to $5x10^5$ pCi ($1.9x10^3$ to $1.9x10^4$ Bq) plutonium-239 dioxide/kg body weight] at 1 and 3 months post-exposure, but not at lower levels (LaBauve et al. 1980). Doserelated increases in the frequency of chromosomal aberrations were observed in Chinese hamster blood cells 30 days after exposure of the animals to plutonium at deposited levels of $1x10^7$ to $2.6x10^8$ pCi ($3.7x10^5$ to $9.6x10^6$ Bq) plutonium-239 dioxide/g of lung tissue (Brooks et al. 1976a).

2.2.1.8 Cancer

Epidemiological studies of occupational cohorts exposed to plutonium have been conducted at two plutonium processing plants, the Los Alamos National Laboratory and the Rocky Flats Nuclear Weapons Plant. A causal link between plutonium exposure and cancer has not been demonstrated in these studies, although there are some suggestions of effects. A prospective mortality study was begun in 1952 on a group of 26 subjects who worked with plutonium at Los Alamos Laboratory during World War II in the Manhattan Project. They have now been studied for 37 years (Voelz et al. 1985). Follow-up has included extensive medical examinations and urine analyses to estimate plutonium body burdens, which showed systemic plutonium deposition ranging from 2,000 to 95,000 pCi (74 to 3,500 Bq) plutonium with a mean of 26,000 pCi ($9.6x10^2$ Bq) plutonium. Mortality in this group as compared to that of United States white males in the general population was significantly less than expected (2.0 vs. 6.6). In addition, no malignant neoplasms have occurred during this extensive period of follow-up. Despite the fact that this study involves only a small number of individuals, it provides information about those who have encountered relatively high plutonium exposures (resulting in deposition of up to 95,000 pCi) and have been followed over a considerable length of time. A study of an additional cohort of 224 Los Alamos male workers was begun in 1974 (Voelz et al. 1983a). Average whole body deposition was estimated at 19,000 pCi (700 Bq) plutonium. Mortality, adjusted for age and year of death, was compared to that of United States males in the general population. Among the cohort, 43 deaths were observed as compared to 77 expected. The number of deaths due to malignant neoplasms among the cohort was also considerably lower than expected (8 vs. 15) including only one lung cancer death vs. five expected.

The studies at the Rocky Flats facility consisted of mortality studies of workers at the plant (Voelz et al 1983b; Wilkinson et al. 1987) and a study of residents living downwind from the facility (Johnson 1981, 1988). Voelz et al. (1983b) reported the results of a study of 7,112 workers employed at the Rocky Flats facility during 1952-1979. Observed deaths were significantly lower than expected (452 vs. 831). Malignant neoplasms were also lower than expected (107 vs. 167).

In a re-analysis of the same Rocky Flats cohort, Wilkinson et al. (i987) investigated mortality patterns among those employed at the facility for at least 2 years. This reduced the cohort size to 5,413 white males. Comparisons of mortality through 1979 were made with expected mortality for United States males in the general population. In addition, employees were ranked according to plutonium body burden, estimated by urinalyses, as either less than 2,000 pCi (74 Bq) or greater than 2,000 pCi (74 Bq) plutonium body burden. Comparisons were made between these two exposure groups. When the cohort with at least 3 years of employment was compared to United States white males, the observed mortality was less than expected. However, the incidences of benign and unspecified neoplasms were greater than expected. These conclusions regarding mortality are in complete agreement with Voelz et al. (1983b). However, when the cohort reported by Wilkinson et al. (1987) was categorized by exposure [less than or greater than 2,000 pCi (74 Bq)] and the two groups compared, it was reported that the group with greater exposure had slightly elevated risk for mortality from all causes of death and from all lymphopoietic neoplasms (Wilkinson et al. 1987). However, the mortality ratios for lung, bone, and liver cancer were not elevated. The authors cautioned that comparisons between the two exposure groups were often based on small numbers of cases, so the precision of these observations is low. There were only four cases of cancers classified as lymphopoietic neoplasms. In addition, they suggested that the results could have been confounded by external radiation exposure (from working in the plutonium facility) or by potential interaction between plutonium radiation and external radiation.

A study of cancer mortality for 1969-1971 in residents near the Rocky Flats facility indicated a somewhat higher incidence than normal for all cancers in individuals living in the areas contaminated with plutonium (Johnson 1981). Tumors of the gonads (testes and ovaries), liver, pancreas, and brain contributed to the higher incidence, whereas the incidences of lung and bone tumors, frequently observed in laboratory animal studies, were not eievated. In a re-analysis of the 1969-1971 data, as well as cancer mortality in 1979-1981 (a more appropriate cancer latency period for the Rocky Flats area contamination), Crump et al. (1987) did not find an increase in the likelihood of developing cancer for those living near the Rocky Flats facility. Crump et al. (1987) attributed the findings of Johnson (1981) to the lack of consideration of confounding urban factors in the design of the study.

Case control studies have been conducted to evaluate the incidence of brain tumors and melanomas, in order to examine the potential associations with plutonium exposure. The study of brain tumors at the Rocky Flats facility and melanomas at Los Alamos did not reveal an association of either disorder with plutonium exposure (Reyes et al. 1983; Acquavella et al. 1983a).

2. HEALTH EFFECTS

Two epidemiology studies have been conducted on a cohort of workers at the Hanford Plant, which produced plutonium in nuclear reactors. Because plutonium exposure was minimal, the studies primarily related to external radiation. Radiation work at Hanford includes reactor operation, chemical separation, fuel fabrication, and research. The radiation is primarily gamma, but also includes neutron, X-radiation, and tritium exposure (Gilbert and Marks 1979). Exposure levels of plutonium were not reported and individuals with plutonium body burdens comprised less than 3% of the cohort. In one study, a cohort of 12,500 white male workers employed at the Hanford Plant for at least 2 years was analyzed for mortality as well as cause of death (Gilbert and Marks 1979). The mean dose was reported to be 4.75 rem. Mortality from all causes was significantiy less than that of United States white males. Death from malignant neoplasms of the pancreas and multiple myeloma occurred at rates higher than expected; deaths from these causes occurred in the group with a dose greater than 15 rem. This correlation was based on a small number of deaths (three each for cancer of the pancreas and multiple myeloma vs. 1 and 0.5 expected, respectively); however, only the increase in the incidence of multiple myeloma was statistically significant.

In a re-evaluation of the Hanford cohort, which included approximately 28,000 male and female workers, Kneale et al. (1981) detected a significant increase in the cancers in radiosensitive tissues in workers exposed to external radiation. Radiosensitive tissues grouped together in their analyses included cancers of the stomach, large intestine, pancreas, pharynx, lung, breast, reticuloendothelial system (lymphoma, myeloma, myeloid leukemia and others), and thyroid. Approximately 50% of these cancers were in the lung; however, smoking histories were not considered in the analysis. Of the male population, only 3% or 225 men had definite evidence of internal radiation. Due to this fact the authors stated that they could safely assume that the incidence of cancer from internal radiation was small compared with that associated with external radiation.

Studies have indicated that plutonium is a lung, skeletal, and liver carcinogen in animals depending on its chemical form, route of exposure, and species. Inhaled plutonium-239 dioxide is insoluble and is retained primarily in the lungs and associated lymph nodes (Muggenburg et al. 1987a; Park et al. 1988). Inhaled plutonium-238 is solubilized and is subsequently translocated from the lung to the bone and liver (Gillett et al. 1988). While the pattern of nonmalignant toxicity among the laboratory species tested was similar (i.e., radiation pneumonitis and pulmonary fibrosis occurred in the higher radiation dose groups in all species tested), species differences in the induction of cancer were apparent. With the exception of Syrian hamsters, cancer developed in animals in the lower exposure groups or in animals that survived initial radiation damage to the lungs.

2. HEALTH EFFECTS

Experiments in dogs have provided the most extensive database on radiation-induced cancer following inhalation exposure to plutonium. The most frequently observed cancer in dogs treated with plutonium-239 dioxide was lung cancer. The majority of lung tumors in dogs were bronchiolar-alveolar carcinomas. In dogs treated with plutonium-238 or the more soluble forms of plutonium-239, such as the nitrate, plutonium translocates from the lungs to other sites, where liver and bone tumors, in addition to lung tumors, have been reported.

Lung tumors were the primary cause of death in dogs exposed to plutonium-239 dioxide at an initial lung deposition as low as 2.1×10^4 pCi (7.8×10^2 Bq) plutonium-239/kg body weight (Muggenburg et al. 1987a; Park et al. 1988). In the study by Park et al. (1988), early deaths among dogs in the highest dose group receiving plutonium-239 resulted from radiation pneumonitis accompanied by respiratory dysfunction, fibrosis, focal hyperplasia, and metaplasia. Increases in the incidence of lung cancer were statistically significant at three lower doses of 6.2×10^3 pCi/kg (2.3×10^2 Bq/kg), 2.4×10^4 pCi/kg (8.9 Bq/kg), and at 8.7×10^4 pCi/kg (3.2×10^3 Bq/kg)/kg body weight. The first lung tumor was found in a dog that died 37 months following exposure; ultimately, after 16 years post-exposure, 55 of the 136 dogs had lung tumors.

With exposure to plutonium-238 dioxide, the primary cause of cancer deaths was osteosarcomas rather than lung tumors. However, lung tumors frequently developed in dogs given a single inhalation exposure to plutonium-238 dioxide resulting in lung deposition levels as low as 1.4×10^3 pCi (5.2×10^1 Bq) plutonium-238/kg body weight (Gillett et al. 1988; Park et al. 1988). In the on-going study by Gillett et al. (1988), of 144 dogs at the beginning of the experiment, 112 died by day 4,000 post-exposure; of these, 100 had osteosarcomas and 28 had lung cancer. With increasing time after exposure, liver lesions increased in severity, with the first liver tumor observed after 3,000 days; the occurrence of primary liver tumors after inhalation exposure to plutonium-238 had not been reported previously.

Osteosarcomas were the principal cause of death among dogs given a single inhalation exposure resulting in deposited levels of 2.3×10^4 to 1.3×10^5 pCi (8.5×10^2 to 4.8×10^3 Bq) plutonium-239 nitrate/kg body weight, although some lung tumors were observed (Dagle et al. 1988). All dogs in the highest exposure group [4.2×10^5 pCi (1.6×10^4 Bq) plutonium-239 nitrate/kg body weight] died of radiation pneumonitis. Cancer mortality in the three lowest exposure groups were comparable to controls.

Statistically significant increases in lung cancer have been reported in rats, with lung deposition levels of 3.1×10^4 pCi (1.1×10^3 Bq) plutonium-238/kg body weight (Sanders et al. 1977) or greater than 3×10^4 pCi (1.1×10^3 Bq) plutonium-239/kg body weight (Sanders and Mahaffey 1979; Sanders et al. 1988). While pulmonary tumors in mice exposed to

plutonium-239 dioxide increased with increasing initial lung deposition, the incidence of lung tumors in any treated group was not statistically significantly different from the untreated controls (Lundgren et al. 1987).

The pulmonary toxicity of plutonium-239 dioxide in Rhesus monkeys and baboons was similar to that of other species; however, they appear to be less sensitive to radiation-induced lung tumors than dcgs and rats. A primary lung tumor occurred in one of nine Rhesus monkeys that survived for 9 years post-treatment (Hahn et al. 1984). Two of 32 baboons developed lung tumors (Metivier et al. 1974) at deposition levels of $2.88x10^5$ to $7.2x10^6$ pCi ($1.06x10^4$ to $2.67x10^5$ Bq) plutonium-239 dioxide/kg body weight; these deposition levels are comparable to those that resulted in lung tumors in dogs.

Syrian hamsters appear to be resistant to lung tumor induction following inhalation of plutonium-239 or plutonium-238 particles. Hamsters were also resistent to radiation-induced lung cancer following exposure to other alpha-emitting radionuclides, such as radon and radon daughters (ATSDR 1990). No statistically significant increases in tumor incidence occurred in lifetime studies in hamsters that had received a single inhalation exposure to plutonium-238 dioxide or plutonium-239 dioxide at lung deposition levels of approximately $1.4x10^6$ to $1.7x10^6$ pCi ($5.2x10^4$ to $6.3x10^4$ Bq) plutonium-238/kg body weight (Mewhinney et al. 1987a; Sanders 1977) or $1.4x10^6$ pCi ($5.2x10^4$ Bq) plutonium-239/kg body weight (Sanders 1977).

Exposure of Syrian hamsters for an intermediate duration (once every other month for a totnl of seven doses over 12 months} to plutonium-239 dioxide, at deposited levels of $1.4x10^4$, $7.1x10^4$, or $3.5x10^5$ pCi ($5.2x10^2$, $2.6x10^3$, or $1.3x10^4$ Bq) plutonium/kg body weight, resulted in several respiratory effects (see Section 2.2.1.2), but no lung tumors were observed in this study (Lundgren et al. 1983). The authors stated that the Syrian hamster may be an inappropriate animal model for lung cancer induction with alpha emitters.

Exposure of mice to plutonium-239 dioxide for an intermediate duration (once every other month for a total of six doses over 10 months) at deposited levels of $1.8x10^4$, $8.1x10^4$, or $4.1x10^6$ pCi ($6.7x10^2$, $3.0x10^3$, or $1.5x10^2$ Bq) plutonium-239/kg body weight resulted in significant lung tumor development in the two lower dose groups (Lundgren et al. 1987). Early mortality precluded tumor development in the highest dose group. Pulmonary tumors (adenomas and adenocarcinomas) were seen in less than 2% of controls but in 13% of low-dose animals and 18% of mid-dose animals.

In a study designed to investigate the effect of temporal dosedistribution, rats were exposed to plutonium-239 dioxide once a month for 3 months with lung deposition levels totaling $8.6x10^4$ pCi ($3.2x10^3$

Bq) plutonium-239/kg body weight, or once a week (for up to 22 weeks) with lung depcsition totaling $1.3x10^5$ to $4.0x10^5$ pCi ($4.8x10^3$ to $1.5x10^4$ Bq) plutonium-239/kg body weight (Sanders and Mahaffey 1961). Lung tumor occurrence ranged from 19 to 60% in treated animals with tumors primarily categorized as adenocarcinomas and squamous carcinomas. No significant difference in lung tumor incidence was observed in mice exposed once a week versus mice exposed once a month for 3 months. Based on total alveolar deposition, a dose-dependent increase in the incidence of all lung tumors was observed. Untreated controls were included in the study, but tumor incidence for these animals was not reported.

2.2.2 Oral Exposure

Exposure by the oral route may occur; however, absorption of plutonium from the gastrointestinal tract appears to be limited (see Section 2.3). Health effects associated with oral exposure to plutonium are presented in Table 2-2 and Figure 2-2.

2.2.2.1 Death

No studies were located regarding death or lifespan shortening in humans after oral exposure to plutonium.

Neonatal rats were given $3.3x10^8$ pCi ($1.2x10^7$ Bq) plutonium-238 citrate/kg body weight by gavage (Fritsch et al. 1987). This single exposure to plutonium resulted in the death of 45% of the treated animals by 2 weeks post-exposure. No deaths were reported in groups given $1x10^5$ pCi ($3.7x10^3$ Bq) plutonium-238/kg (Fritsch et al. 1987).

2.2.2.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, hematological, musculoskeletal, hepatic, renal, or dermal/ocular effects in humans or animals after oral exposure to plutonium.

Gastrointestinal Effects. No studies were located regarding gastrointestinal effects in humans after oral exposure to plutonium.

Gastrointestinal effects were observed in neonatal rats following administration by gavage of $1x10^5$ or $3.3x10^8$ pCi ($3.7x10^3$ or $1.2x10^7$ Bq) plutonium-238 citrate/kg body weight (Fritsch et al. 1987). In the lower treatment group, mild hypertrophy of the crypts of the small intestine, which form the secretions of the small intestine, was observed 11 days post-exposure. Total disappearance of epithelial cells and crypts, combined with intestinal hemorrhaging, was observed in the higher treatment group, also sacrificed at 11 days. However, neonatal rodents have immature and poorly enclosed crypts in the small intestine,

TABLE 2-2. Levels of Significant Exposure to Plutonium - Oral

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (pCi/kg)	LOAEL (Effect) Less Serious (pCi/kg)	LOAEL (Effect) Serious (pCi/kg)	Reference	Chemical Species
ACUTE EXPOSURE								
Death								
1	Rat	(G) 1d		$1.0x10^5$		$3.0x10^8$	Fritsch et al. 1987	^{238}Pu citrate
Systemic								
2	Rat	(G) 1d	Gastro		$1.6x10^{11}$ (path change)		Sullivan et al. 1960	$^{239}PuO_2$
3	Rat	(G) 1d	Gastro		$1.0x10^5$ (hypertrophy)	$3.3x10^8$ (intestinal hemor)	Fritsch et al. 1987	^{238}Pu citrate
			Other	$1.0x10^5$		$3.3x10^8$ (growth inhibit)		

d = day; (G) = gavage; Gastro = gastrointestinal; hemor = hemorrhaging; inhibit = inhibition; LOAEL = lowest observed adverse effect level; NOAEL = no observed adverse effect level; path = pathological

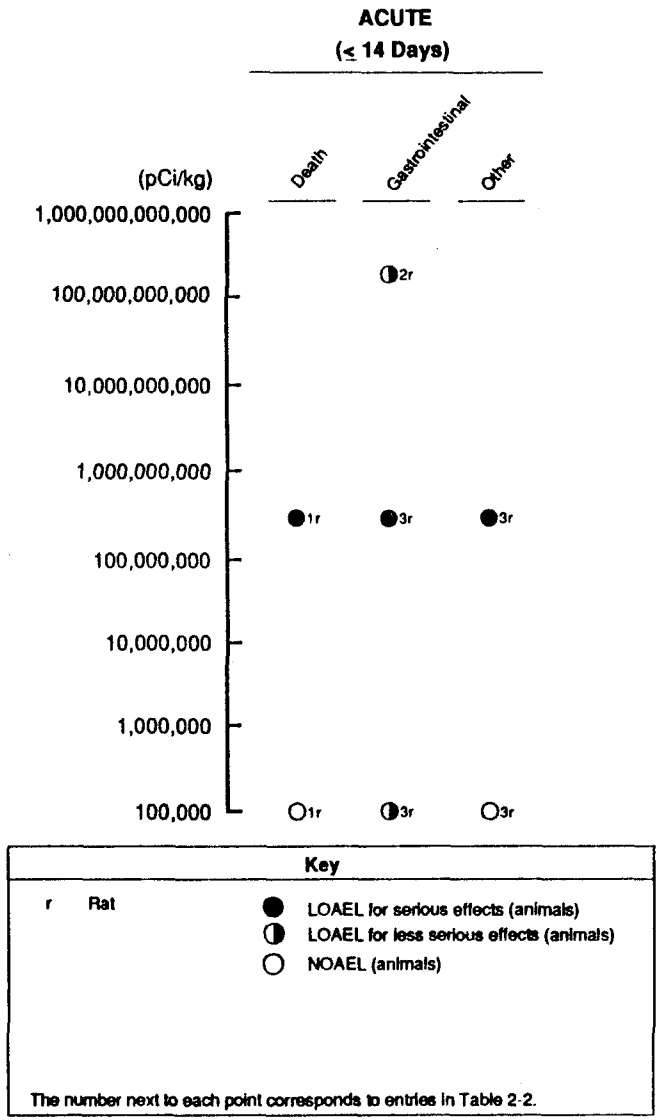

FIGURE 2-2. Health Effects Associated with Plutonium Deposition - Oral

which is the main site of plutonium retention following oral exposure (see Section 2.3.2.4), as compared to other neonatal mammals. Therefore, neonatal rats could be expected to be more sensitive to the radiologic effects of plutonium than other neonates or adult mammals (Fritsch et al. 1987). Gastrointestinal effects have also been observed in adult rats given $1.6x10^{11}$ pCi ($5.7x10^{9}$ Bq) plutonium-239 dioxide/kg body weight. At 3 days post-exposure, there was an increase in neutrophils on the surface epithelium and superficial cellular layers of the large intestine (Sullivan et al. 1960). At 6 days post-exposure this increase was no longer observed.

Other Systemic Effects. No studies were located regarding other effects in humans or animals after oral exposure to plutonium. No studies were located regarding the following health effects in humans or animals after oral exposure to plutonium.

2.2.2.3 Immunological Effects

2.2.2.4 Neurological Effects

2.2.2.5 Developmental Effects

2.2.2.6 Reproductive Effects

2.2.2.7 Genotoxic Effects

2.2.2.8 Cancer

2.2.3 Dermal Exposure

2.2.3.1 Death

No studies were located regarding death or the shortening of lifespan in humans or animals after dermal exposure to plutonium.
2.2.3.2 Systemic Effects

No studies were located regarding respiratory, cardiovascular, gastrointestinal, hematological, musculoskeletal, hepatic, renal, or dermal/ocular effects in humans or animals after dermal exposure to plutonium.

No studies were located regarding the following health effects in humans or animals following dermal exposure to plutonium.

2.2.3.3 Immunological Effects

2.2.3.4 Neurological Effects

2.2.3.5 Developmental Effects

2.2.3.6 Reproductive Effects

2.2.3.7 Genotoxic Effects

2.2.3.8 Cancer

2.2.4 Other Routes of Exposure

Health effects associated with plutonium administered by injection are presented in Table 2-3 and Figure 2-3.

2.2.4.1 Death

No studies were located regarding death or lifespan shortening in humans after exposure to plutonium by other routes.

A significant decrease in lifespan was observed in rats, mice, and hamsters following a single injection of plutonium-239 at concentrations . ranging from $2x10^5$ to $7.5x10^7$ pCi ($7.4x10^3$ to $2.8x10^6$ Bq) plutonium-239/kg body weight given as the citrate (intravenous) or dioxide (intraperitoneal) (Ballou et al. 1967; Brooks et al. 1983; Sanders 1973a; Svoboda et al. 1980a, 1980b). Survival times decreased with increasing doses in rats and hamsters (Brooks et al. 1983; Sanders 1973a). Death resulted from bone marrow hypoplasia in hamsters approximately 400 days following an intravenous exposure [2x107 pCi ($7.4x10^5$ Bq) plutonium-239 citrate/kg body weight] (Brooks et al. 1982). In rats injected intraperitoneally at concentrations up to $8.3x10^6$ pCi ($3.1x10^5$ Bq) plutonium-239 dioxide/kg body weight, death resulted mainly from large malignant abdominal tumors accompanied by hemorrhage-induced anemia approximately 350 to 580 days post-exposure (Sanders 1973a).

An age-dependent effect on lethality was observed in rats injected intravenously with $6x10^6$ to $9x10^7$ pCi ($2.2x10^5$ to $3.3x10^6$ Bq) plutonium-239/kg body weight as the monomeric (citrate) or polymeric (nitrate) forms (Mahlum and Sikov 1974). Neonates were more susceptible to the lethal effects of the monomeric form of plutonium-239, while adults and weanlings were more susceptible to the polymeric form.

Animal studies indicate that the polymeric (nitrate) forms of plutonium-239 and plutonium-238 are more acutely toxic than the corresponding monomeric (citrate) forms (see Section 2.3.2.4). In rats, 30-day LD_{50}s for the monomeric [$9.7x10^7$ pCi ($3.6x10^6$ Bq)/kg] and

TABLE 2-3. Health Effects Associated with Plutonium Administration - Other Routes of Exposure

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (pCi/kg)	LOAEL (Effect) Less Serious (pCi/kg)	LOAEL (Effect) Serious (pCi/kg)	Reference	Chemical Species
ACUTE EXPOSURE								
Death								
1	Rat	(IV) 1d		$1.3x10^8$			Ballou et al. 1967	^{238}Pu citrate
2	Rat	(IV) 1d				$9.7x10^7$ (30 day LD50)	Mahlum and Sikov 1974	^{239}Pu citrate
3	Rat	(IV) 1d				$9.8x10^7$ (30 day LD50)	Mahlum and Sikov 1969a	^{238}Pu nitrate
4	Rat	(IV) 1d				$1.6x10^8$ (30 day LD50)	Mahlum and Sikov 1969a	^{238}Pu citrate
5	Rat	(IV) 1d				$4.7x10^7$ (30 day LD50)	Mahlum and Sikov 1974	^{239}Pu nitrate
6	Rat	(IV) 1d				$7.9x10^7$ (dec lifespan)	Ballou et al. 1967	^{239}Pu citrate
7	Mouse	(IV) 1d				$4.9x10^6$ (dec lifespan)	Svoboda et al. 1980a	^{239}Pu citrate
8	Hamster	(IV) 1d				$2.0x10^6$ (dec lifespan)	Brooks et al. 1983	^{239}Pu citrate
Systemic								
9	Human	(IV) 1d	Hemato	$7.3x10^3$			Langham et al. 1980	^{238}Pu or ^{239}Pu citrate
10	Rat	(IP) 1d	Resp	$8.3x10^6$			Sanders 1975a	$^{239}PuO_2$
11	Rat	(IV) 1d	Musc/skel			$1.8x10^7$ (dec break strength)	Sikov and Mahlum 1976	^{239}Pu citrate
12	Rat	(IV) 1d	Hemato			$3.6x10^7$ (dec WBC & RBC count)	Ballou et al. 1967	^{238}Pu citrate
			Hepatic			$7.5x10^7$ (liver damage)		

TABLE 2-3 (continued)

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (pCi/kg)	LOAEL (Effect) Less Serious (pCi/kg)	LOAEL (Effect) Serious (pCi/kg)	Reference	Chemical Species
13	Rat	(IP) 1d	Resp Hemato			2.0×10^5 (pneumonitis) 8.2×10^6 (lymphopenia)	Sanders 1973a	$^{239}PuO_2$
14	Mouse	(IV) 1d	Hemato			3.6×10^5 (dec stem cells)	Svoboda et al. 1987	^{239}Pu citrate
15	Hamster	(IV) 1d	Hepatic			2.0×10^6 (hep degener)	Benjamin et al. 1976	^{239}Pu citrate
16	Dog	(IV) 1d	Musc/skel	3.0×10^5		1.0×10^6 (fractures)	Taylor et al. 1962	^{239}Pu citrate
17	Dog	(SB) 1d	Derm/oc			9.8×10^4 (scarring)	Dagle et al. 1984	^{239}Pu nitrate
18	Dog	(IV) 1d	Hemato	9.0×10^5		2.9×10^6 (dec lymphocytes)	Dougherty and Rosenblatt 1971	^{239}Pu citrate
19	Dog	(IV) 1d	Musc/skel	1.0×10^5			Bruenger et al. 1978	^{239}Pu citrate
20	Dog	(IV) 1d	Hepatic			3.0×10^6 (func impair)	Cochran et al. 1962	^{239}Pu citrate
21	Dog	(IV) 1d	Hepatic	6.3×10^2	1.9×10^3 (nodules)		Taylor et al. 1986	^{239}Pu citrate
Immunological								
22	Dog	(SB) 1d				7.5×10^5 (scarred lymph nodes)	Dagle et al. 1984	^{239}Pu oxide
Developmental								
23	Rabbit	(IV) 9,15,27,9 15-28 Gd				1.0×10^7 (fetal lethal)	Kelman et al. 1982a	^{239}Pu citrate

TABLE 2-3 (continued)

Figure Key	Species	Exposure Frequency/ Duration	Effect	NOAEL (pCi/kg)	LOAEL (Effect) Less Serious (pCi/kg)	LOAEL (Effect) Serious (pCi/kg)	Reference	Chemical Species
Cancer								
24	Rat	(IT) 1d				$8.2x10^4$ (CEL-lung)	Sanders 1975b	$^{239}PuO_2$
25	Rat	(IV) 1d				$3.0x10^5$ (CEL-skeletal)	Sikov et al. 1978a	^{239}Pu citrate
26	Rat	(IP) 1d				$2.0x10^5$ (CEL-abdominal)	Sanders 1973	$^{239}PuO_2$
27	Rat	(IP) 1d				$3.6x10^6$ (CEL-mammary)	Sanders 1974	$^{238}PuO_2$
28	Mouse	(IP) 1d				$3.2x10^6$ (CEL-skeletal)	Taylor et al. 1983	^{239}Pu citrate
29	Mouse	(IV) 1d				$4.9x10^6$ (CEL-leukemia)	Svoboda et al. 1981	^{239}Pu citrate
30	Hamster	(IV) 1d				$2.0x10^6$ (CEL-skeletal, liver)	Brooks et al. 1983	^{239}Pu citrate
31	Dog	(IV) 1d				$1.0x10^4$ (CEL-skeletal)	Mays et al. 1987	^{239}Pu citrate
32	Dog	(IV) 1d				$1.9x10^3$ (CEL-liver)	Taylor et al. 1986	^{239}Pu citrate
INTERMEDIATE EXPOSURE Cancer								
33	Mouse	(IP) 8 wk 2 d/wk 16 d				$5.0x10^4$ (CEL-leukemia)	Humphreys et al. 1987	^{239}Pu nitrate

break = breaking; CEL = cancer effect level; d = day; dec = decreased; Derm/oc = dermal/ocular; func impair = functional; Hemato = hematological; hep degener = hepatic degeneration; (IP) = intraperitoneal; (IT) = intratracheal; (IV) = intravenous; LD50 = dose which produces lethal effects in 50% of the animals; LOAEL = lowest observed adverse effect level; Musc/skel = musculoskeletal; NOAEL = no observed adverse effect level; RBC = red blood cell; Resp = respiratory; (SB) = subcutaneous; WBC = white blood cell; wk = week

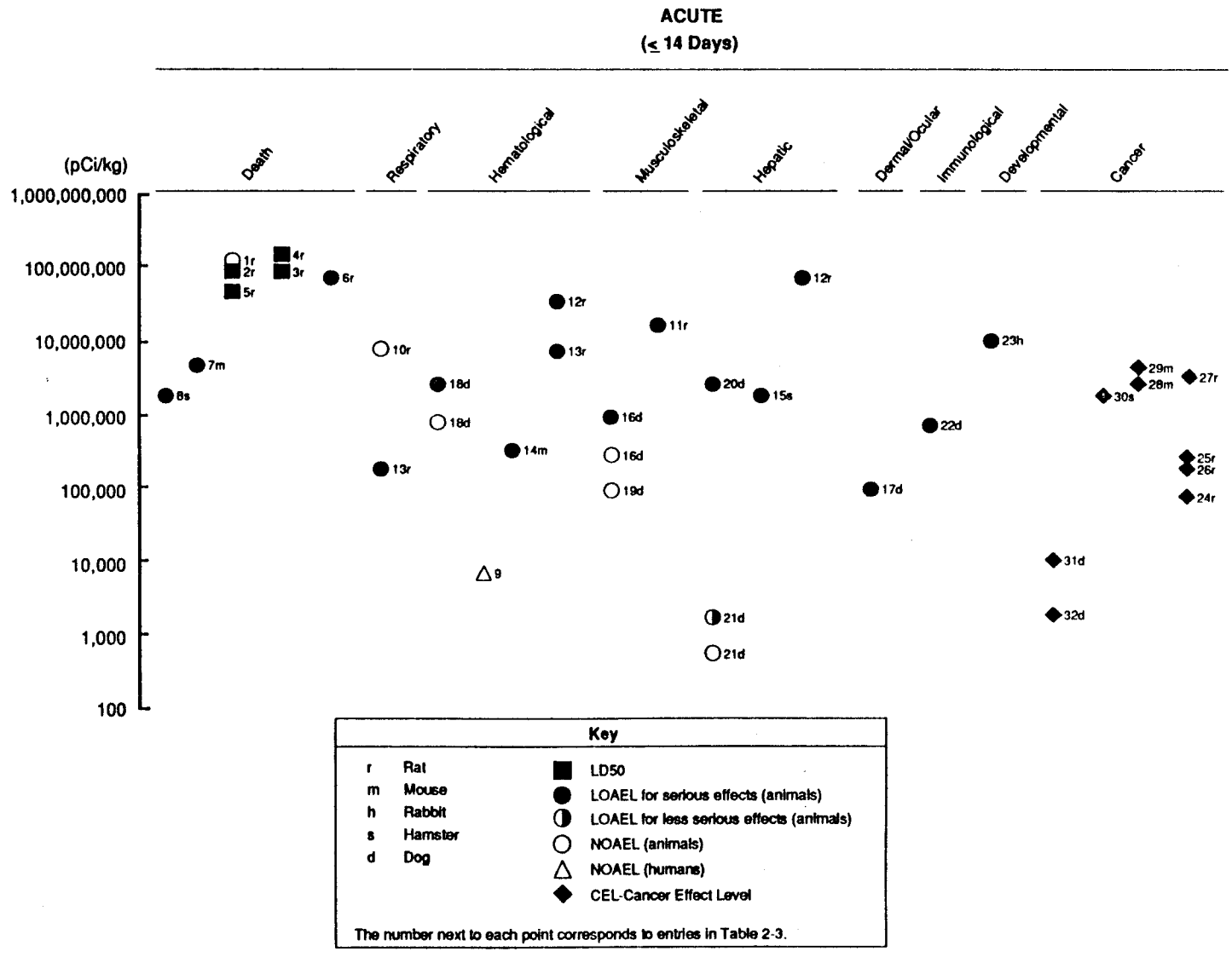

FIGURE 2-3. Health Effects Associated with Plutonium Deposition - Other Routes of Exposure

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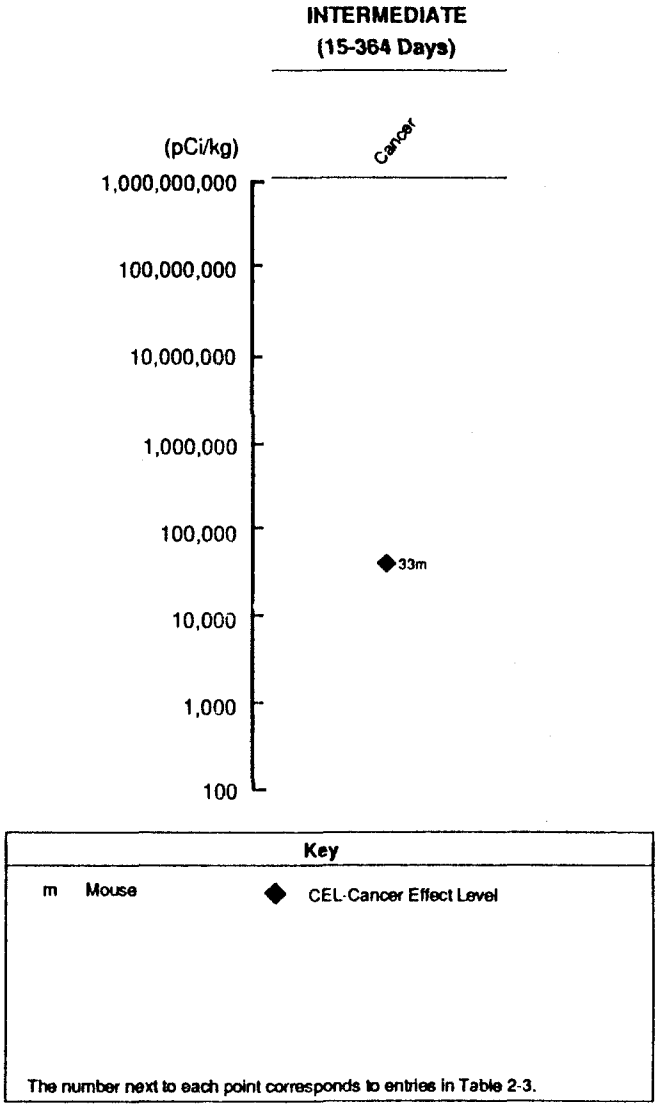

FIGURE 2-3 (Continued)

polymeric [4.7×10^7 pCi (1.7×10^6 Bq)/kg] forms of plutonium-239 were lower than 30-day LD_{50}s for the corresponding forms of plutonium-238 [monomeric, 1.6×10^8 pCi (5.9×10^6 Bq)/kg; polymeric, 9.8×10^7 pCi (3.6×10^6 Bq)/kg] (Mahlum and Sikov 19696; 1974).

Plutonium-239 is more acutely toxic than an equivalent picocuric amount of plutonium-238 (Ballou et al. 1967). Survival times in rats given a single intravenous injection of 7.9x10' to 1.3×10^8 pCi ($2.9 \times 10^6$to 4.8×10^6 Bq) plutonium-239 citrate/kg body weight were decreased, while survival times of rats administered equivalent amounts, on a radioactivity basis, of plutonium-238 citrate were not reduced (Ballou et al. 1967).

2.2.4.2 Systemic Effects

No studies were located regarding cardiovascular or gastrointestinal effects in humans or animals after exposure to plutonium by other routes.

Respiratory Effects. No studies were located regarding respiratory effects in humans after exposure to plutonium by other routes. Increases in the incidence of pneumonitis, inflammation, and edema were observed in the lungs of rats following administration of 2×10^5 pCi (7.4×10^3 Bq) plutonium-239 dioxide/kg body weight as a single intraperitoneal injection (Sanders 1973a). However, the statistical significance of these increases in respiratory effec,ts could not be determined based on the reported data.

Hematological Effects. No acute effects, as measured by evaluation of hematological end points, occurred in a case study of 18 humans following a single intravenous injection at levels ranging from 4×10^3 to 7.3×10^3 pCi (1.5×10^2 to 2.7×10^2 Bq) plutonium-238 or -239 citrate/kg body weight (Langham et al. 1980). (While reported in a memorial publication that republished Dr. Langham's work, this particular study was conducted in the early 1950s.) Thirty years following exposure to plutonium, 4 of the 18 individuals were still alive. One case could not be located for follow-up. The authors reported that plutonium could not be considered a contributing factor to the cause of death in the 13 cases (Rowland and Durbin 1976).

Anemia was observed in laboratory animals following a single injection of plutonium-238 or -239. Rats given a single intraperitoneal injection of plutonium-239 dioxide [8×10^6 pCi (3.0×10^5 Bq)/kg] or a single intravenous injection of plutonium-238 citrate [3.6×10^7 pCi (1.3×10^6 Bq)/kg] developed,anemia (Ballou et al. 1967; Sanders 1973a; Sanders and Jackson 1972). In rats exposed intravenously, a decrease in viable bone marrow with replacement of marrow by a calcified plug

accompanied the anemia (Ballou et al. 1967). Anemia, characterized by decreases in red blood cell volume, accomranied by increases in the number of new red blood cells (reticulocvtes), was observed in dogs exposed to a single intravenous injection of $2.9x10^6$ pCi ($1.1x10^5$ Bq) plutonium-239 citrate/kg (Dougherty and Rosenblatt 1971).

A decrease in the number of white blood cells, which continued to decrease with time post-exposure, was observed in rats given a single intravenous injection of $3.6x10^7$ pCi ($1.3x10^6$ Bq) plutonium-238 citrate/kg (Ballou et al. 1967). Lymphopenia was observed in rats given a single intraperitoneal injection of $8.2x10^6$ pCi ($3.0x10^5$ Bq) plutonium-239 dioxide/kg (Sanders 1973a; Sanders and Jackson 1972). Decreased white blood cell counts were also observed in dogs given a single intravenous injection of $2.9x10^6$ pCi ($3.7x10^3$ Bq) plutonium-239 citrate/kg (Dougherty and Rosenblatt 1971).

Svoboda and co-workers (1979, 1980a, 1980b, 1982a, 1983, 1985, 1987) have conducted extensive research on mice concerning the effects of plutonium-239 on stem cells, the blood producing cells of the bone marrow. These effects on bone marrow are considered to be "preleukemic" by these authors (Svoboda and Kotaskova 1982). Administration of monomeric plutonium-239 citrate [$3.6x10^5$ pCi ($1.3x10^4$ Bq)/kg] as a single intravenous injection resulted in a decrease in the number of hematopoietic stem cells of the bone marrow in mice as soon as 4 weeks after exposure (Svoboda et al. 1987). This initial damage in one portion of the bone marrow appeared to be partially compensated, as exhibited by a slight increase in the number of stem cells (due to increased proliferative activity) in another part of the tissue by approximately 30 weeks post-exposure; however, the number of stem cells was still less than the number observed in untreated controls (Svoboda and Kotaskova 1982; Svoboda et al. 1979). The authors hypothesize that persistent radiological damage to the stem cells from plutonium-239 may lead to an early stage of leukemia (Svoboda and Kotaskova 1982). A similar decrease in stem cells was reported in mice given a single intravenous injection of polymeric plutonium-239 nitrate [5x106 to $1.5x10^7$ pCi ($1.9x10^5$ to $5.6x10^5$ Bq)/kg] (Joshima et al. 1981).

Musculoskeletal Effects. No studies were located regarding musculoskeletal effects in humans after exposure to plutonium by,other routes.

Increased numbers of spontaneous fractures occurred in dogs given a single intravenous injection of $1x10^5$ to $3x10^6$ pCi ($3.7x10^3$ to $1.1x10^5$ Bq) plutonium-239 citrate/kg body weight (Ta, et al. 1962). Total incidence of fractures decreased with decrea: dose with only one fracture observed in the two lowest treatment groups [$lx10^5$ and $3x10^5$ pCi ($3.7x10^3$ and $1.1x10^4$ Bq) plutonium-239/kg] combined.

The anatomical range of the fractures increased with increasing dose. Plutonium exposure did not result in growth retardation in neonatal dogs as measured by the growth of long bones (Bruenger et al. 1978).

Age-dependent differences in the musculoskeletal effects induced by plutonium have been observed in adult, weanling, and neonatal rats given single intravenous injections of plutonium at concentrations ranging from $6x10^6$ to 9x107 pCi ($2.2x10^5$ to $3.3x10^6$ Bq) plutonium-239/kg body weight, administered in the monomeric or the polymeric forms (Mahlum and Sikov 1969b; Sikov and Mahlum 1976). Weanlings were more susceptible to the musculoskeletal effects of plutonium (Mahlum and Sikov 1?69b), possibly due to the rapid growth of the bone cells, and greater radiosensitivity of these cells to plutonium. An increase in the incidence of spontaneous fractures was observed in weanlings, but not in adults or neonates, given the monomeric form of plutonium-239 (Sikov and Mahlum 1976). A decrease in the breaking strength of the femur was observed in weanling and adult rats, but was more pronounced in weanlings (Sikov and Mahlum 1976). In neonatal rats, the only musculoskeletal effects, which were mild and sporadic, were observed in the higher treatment groups administered greater than $6x10^7$ pCi ($2.2x10^6$ Bq)/kg (Sikov and Mahlum 1976; Mahlum and Sikov 1969b).

Hepatic Effects. No studies were located regarding hepatic effects in humans after exposure to plutonium by other routes.

Hepatic damage was observed in rodents after a single intravenous injection of high levels of plutonium. Severe hepatic degeneration occurred in hamsters observed for life following administered levels as low as $2x10^6$ pCi ($7.4x10^4$ Bq) plutonium-239 citrate/kg body weight (Benjamin et al. 1976). A single intravenous injection of $7.5x10^7$ pCi ($2.8x10^6$ Bq) plutonium-239 citrate/kg resulted in damage to the liver parenchyma of rats as early as 15 days post-exposure (Ballou et al. 1967).

In studies in which dogs were given a single intravenous injection of plutonium-239 citrate, hepatic effects were observed to be doserelated. No hepatic effects were reported in dogs given 630 pCi (23 Bq) plutonium/kg body weight (Taylor et al. 1986), while gross and microscopic liver nodules and/or hyperplasia were observed by year 8 following injection of $1.9x10^3$ to $3x10^5$ pCi ($7.0x10^1$ to $1.1x10^4$ Bq) plutonium-239/kg (Cochran et al. 1962; Taylor et al. 1986). At higher levels [$1x10^6$ and $3x10^6$ pCi ($3.7x10^4$ and $1.1x10^5$ Bq) plutonium-239/kg], functional impairment of the liver was observed 4 years post-exposure (Cochran et al. 1962). Some of the animals at the highest treatment level [$3x10^6$ pCi ($1.1x10^5$ Bq)/kg] had functional impairment, as well as shrunken livers and ascites, which the authors described as indicative of decompensated cirrhosis .(Cochran et al. 1962).

Renal Effects. No studies were located regarding renal effects in humans after exposure to plutonium by other routes.

Mild to severe chronic nephritis was observed in Sprague-Dawley rats following a single intraperitoneal injection of $2x10^5$ pCi ($7.4x10^3$ Bq) plutonium-239 dioxide (Sanders 1973a). However, the statistical significance of these renal effects could not be determined based on the reported data. In addition, renal nephritis may be a common occurrence in the strain of rats used in this study.

Dermal/Ocular Effects. No studies were located regarding dermal/ocular effects in humans after exposure to plutonium by other routes.

Loss of hair, thickening of the dermis, and focal scarring were observed around subcutaneous implants of plutonium-239 in dogs administered plutonium dioxide [$7.5x10^5$ pCi ($2.8x10^4$ Bq)/kg] or plutonium nitrate [$9.8x10^4$ pCi ($3.6x10^3$ Bq)/kg] (Dagle et al. 1984). These effects may have resulted from exposure to plutonium; however, the statistical significance of these dermal effects could not be determined based on the reported data.

Other Systemic Effects. Other systemic effects have been observed in rats following a single injection of plutonium. Mesothelial hyperplasia was observed in rats injected intraperitoneally with $8x10^6$ pCi ($3.0x10^5$ Bq) plutonium-239 dioxide/kg (Sanders and Jackson 1972). A single intravenous injection of $6x10^5$ to $9x10^7$ pCi ($2.2x10^5$ to $3.3x10^6$ Bq) plutonium-239 citrate/kg, administered as either the monomeric or polymeric form, resulted in a sex-related decrease in weight gain in weanling rats; the decrease in weight gain in males occurred at a lower level [$6x10^5$ pCi ($2.2x10^4$ Bq)/kg] than in females ($1.8x10^7$ pCi ($6.7x10^5$ Bq)/kg] (Mahlum and Sikov 1974). As seen with musculoskeletal effects (see previous section), weanlings were more susceptible to a decrease in weight gain following exposure to plutonium than adults or neonates. A decrease in weight gain was observed in adult rats following a single intravenous injection of $1.8x10^7$ pCi ($6.7x10^5$ Bq) plutonium-239/kg or greater, administered in the monomeric form, but was not observed following administration of the polymeric form. Decreased weight gain in neonatal rats was observed only following lethal doses of plutonium-239 (Mahlum and Sikov 1974).

2.2.4.3 Immunological Effects

No studies were located regarding immunologic effects in humans after exposure to plutonium by other routes.

Effects on some tissues of the immune system have been observed in dogs following a single subcutaneous injection of 7.4×10^5 pCi (2.7×10^4 Bq) plutonium-239 dioxide/kg (Dagle et al. 1984). The regional lymph nodes, which drained the injection sites of plutonium, were reduced in size in six of eight dogs exposed and in five of the dogs the lymph nodes consisted of only scar tissue (Dagle et al. 1984).

2.2.4.4 Neurological Effects

No studies were located regarding neurological effects in humans or animals after exposure to plutonium by other routes.

2.2.4.5 Developmental Effects

No studies were located regarding developmental effects in humans after exposure to plutonium by other routes.

Rabbits were given a single intravenous injection of 1×10^7 or 4×10^7 pCi (3.7×10^5 or 1.5×10^6 Bq) plutonium-239/kg, administered in the monomeric form, on various days of gestation (Kelman et al. 1982a). Fetal weights of the offspring of does given 4×10^7 pCi (1.5×10^6 Bq) plutonium-239/kg were significantly decreased compared to the fetal weights of the offspring of does given 1×10^7 pCi (3.7×10^5 Bq) plutonium-239/kg or the offspring of untreated controls. In contrast, fetal weights of does given 1×10^7 pCi (3.7×10^5 Bq) plutonium-239/kg were significantly increased above controls. The number of litters containing dead fetuses was significantly increased in the group of dams given 1×10^7 pCi (3.7×10^5 Bq) plutonium-239/kg on gestation days 15 to 28. Rabbits given either 1×10^7 or 4×10^7 pCi (3.7×10^5 or 1.5×10^6 Bq)/kg on gestation days 9 to 28 had significantly fewer fetuses. No teratogenic effects of plutonium-239 were observed (Kelman et al. 1982a).

2.2.4.6 Reproductive Effects

No studies were located regarding reproductive effects in humans after exposure to plutonium by other routes.

In mice, dominant lethality has been shown to result from plutonium exposure. Fetal intrauterine deaths occurred in female mice mated with male mice treated 4 weeks prior to mating. Male mice were given (intravenously) plutonium-239 at levels ranging from 1.6×10^6 to 1.6×10^7 pCi (5.9×10^4 to 5.9×10^5 Bq) plutonium-239/kg body weight (Lüning et al. 1976a, 1976b). The effects of the dominant lethal mutations were also observed when untreated females were mated with male mice from the Fl generation. Exposure of male mice to higher doses of plutonium-239 resulted in sterility 12 weeks post-exposure (Lüning et al. 1976a, 1976b). Exposure of female mice to plutonium also resulted in dominant lethal mutations (Searle et al. 1982). Female mice intravenously

injected with $2x10^7$ pCi ($7.4x10^5$ Bq) plutonium-239 citrate/kg body weight exhibited a marked oocyte killing which resulted in a reduction in the number of mice which became pregnant, compared with the controls. Both pre- and post-implantation dominant lethals were induced at long periods (12 weeks) after intravenous exposure to plutonium.

2.2.4.7 Genotoxic Effects

Open wounds represent a significant route through which plutonium workers might be exposed to plutonium alpha-particles. Chromosomal aberrations were observed in lymphocytes among 8 plutonium workers in the United Kingdom occupationally exposed to plutonium with the primary routes of exposure through wounds, punctures, or abrasions [estimated body burdens from $2.1x10^4$ to $4x10^4$ pCi ($7.8x10^2$ to $1.5x10^3$ Bq) plutonium, based on urine analyses]. In exposed individuals the number of dicentric aberrations averaged 5 per 500 cells, while the natural population background frequency of this aberration is 1 per 4,000 cells (Schofield 1980; Schofield et al. 1974).

Increased chromosomal aberrations were observed in liver tissue of Chinese hamsters intravenously given plutonium-239 or plutonium-238, as the citrate or the dioxide, to achieve levels ranging from $7x10^2$ to $2x10^4$ pCi ($2.6x10^1$ to $7.4x10^2$ Bq) plutonium-239 or plutonium-238/g of liver tissue (Brooks et al. 1976a) or $2x10^6$ pCi ($7.4x10^4$ Bq) plutonium-239 citrate/kg of body weight (Benjamin et al. 1976). The frequency of aberrations was much higher in hamsters exposed by intravenous injection to plutonium-239 or plutonium-238 citrate, than in hamsters exposed to plutonium-239 or plutonium-238 dioxide (Brooks et al. 1976b). No statistically significant increases in the incidence of chromosomai aberrations per spermatogonia cell were observed in mice or hamsters following intravenous administration of plutonium-239 citrate [$2x10^3$ pCi ($7.4x10^1$ Bq) plutonium-239/kg body weight], compared to untreated controls (Brooks et al. 1979).

Other genetic effects attributed to plutonium are dominant lethality and chromosome translocations in spermatocytes. Fetal intrauterine death occurred in female mice mated with male mice treated 4 weeks prior to mating. Male mice were given (intravenously) plutonium-239 at levels ranging from $1.6x10^6$ to $1.6x10^7$ pCi (5.9x104 to $5.9x10^5$ Bq) plutonium-239/kg body weight (Lüning et al. 1976a, 1976b). The effects of the dominant lethal mutations were also observed when untreated females were mated with male mice from the Fl generation. Exposure of male mice to higher doses of plutonium-239 resulted in sterility 12 weeks post-exposure (Lüning et al. 1976a, 1976b).

Increased frequency of reciprocal translocations in spermatogonia was observed in male mice 6 to 18 weeks after intravenous injection of $1x10^7$ pCi ($3.7x10^5$ Bq) plutonium-239 citrate/kg body weight (Beechey et al. 1975). An increase in the frequency of heritable translocations was

also observed in male mice intravenously injected with $1x10^7$ pCi ($3.7x10^5$ Bq) plutonium-239 citrate/kg body weight (Generoso et al. 1985). The frequency of translocations increased as a function of time and dose. However, induction of reciprocal translocations was not significant in male mice intravenously injected with $4x10^6$ pCi ($1.5x10^5$ Bq) plutonium-239/kg body weight (Searle et al. 1976).

Exposure of mice to $3.6x10^5$ pCi ($1.3x10^4$ Bq) plutonium-239 citrate/kg body weight resulted in increased chromosomal aberrations in bone marrow cells (Svoboda et al. 1987). The highest incidence of these mutations was observed in the early days following exposure to plutonium.

2.2.4.8 Cancer

No studies were located regarding cancer effects in humans after exposure to plutonium by other routes.

Following a single intravenous injection of plutonium-239 citrate, osteosarcomas were found in mice [$3.2x10^5$ pCi ($1.2x10^4$ Bq)/kg] (Taylor et al. 1983), rats [$3x10^5$ pCi (1:$1x10^4$ Bq)/kg] (Sikov et al. 1978a), hamsters [$2x10^6$ pCi ($7.4x10^4$ Bq)/kg] (Brooks et al. 1983), and dogs [$1x10^4$ pCi ($3.7x10^2$ Bq)/kg] (Mays et al. 1987). Latency periods for the induction of these bone tumors were not reported. However, lifespan was significantly shortened only in hamsters. Lifespan studies in beagle dogs provided evidence that certain skeletal sites were more prone to develop plutonium-induced osteosarcomas than others (Miller et al. 1986). In these dogs, most osteosarcomas originated in trabecular (spongy) bone areas, such as the ends of long bones, the pelvis, vertebrae, and the area surrounding the marrow of the bone (endosteal surfaces) (Miller et al. 1986). Because these areas may have a greater blood flow, a greater amount of plutonium may deposit in these areas of the bone (see Section 2.3.2.4).

Induction of osteosarcomas following a single injection of plutonium-239 appeared to be age-dependent as well as sex-dependent. A statistically significant increase in the incidence of bone tumors was observed in adult and weanling rats given a single intravenous injection of $3x10^5$ pCi ($1.1x10^4$ Bq) plutonium-239 citrate/kg (Sikov et al. 1978a). At higher levels [$3x10^6$ to $3x10^7$ pCi ($1.1x10^5$ to $1.1x10^6$ Bq) plutonium-239/kg via intracardiac injection], a nonsignificant increase in the incidence of bone tumors was observed in neonatal rats. The anatomical distribution of these bone tumors was markedly influenced by age at time of injection. In neonates one-third of all tumors were in the head while older groups had bone tumors primarily in the extremities or vertebrae (Sikov et al. 1978a). A statistically significant increase in the incidence of bone t'umors was observed in female mice, but not in male mice given a single intraperitoneal injection of plutonium-239 citrate (9x105 pCi ($3.3x10^4$ Bq)/kg] (Taylor et al. 1981a). Females may

be more sensitive to the toxic bone effects following a single exposure to plutonium-239 because the induction of osteosarcomas could be estrogen related (Taylor et al. 1981a).

Liver tumors have been observed in dogs following a single intravenous injection of plutonium-239. A statistically significant increase in the incidence of hepatic tumors, mostly bile duct tumors, has been observed in dogs given 1.9×10^{3} pCi (7.0×10^{1} Bq) plutonium-239 citrate/kg body weight (Taylor et al. 1986). These tumors were observed primarily in the lower dose groups following long latency periods. Most of the liver tumors observed were in dogs sacrificed due to bone cancer; however, liver tumors were primary liver tumors and not metastases.

Liver and bone tumors were observed in hamsters administered a single intravenous injection of 2×10^{6} pCi (7.4×10^{4} Bq) plutonium-239/kg body weight, administered as plutonium citrate (monomeric) (Brooks et al. 1983). However, in hamsters given a single intravenous injection of 2×10^{6} pCi (7.4×10^{4} Bq) plutonium-239 dioxide/kg (polymeric), a significant increase in the incidence of liver tumors was observed with no accompanying bone tumors (Brooks et al. 1983).

No conclusive evidence exists that plutonium induces leukemia in laboratory animals. However, in mice with a high spontaneous incidence of leukemia (ICR mice), administration of plutonium as a single intravenous injection [4.4×10^{6} pCi (1.8×10^{5} Bq) plutonium-239 citrate/kg] decreased the latency period for the appearance of leukemia (Svoboda et al. 1981).

Various types of tumors have been observed in rats following a single intraperitoneal injection of plutonium dioxide. A dose-dependent increase in the incidence of mesotheliomas and soft-tissue sarcomas was observed in rats given 2×10^{5} to 8×10^{6} pCi (7.4×10^{3} to 3.0×10^{5} Bq) plutonium-239 dioxide/kg (Sanders 1973). Death in many of the treated rats resulted from large malignant abdominal tumors. It appears that plutonium-239 particles, administered as plutonium dioxide, can produce mesotheliomas in the abdominal cavity, but a greater radiation dose is needed to induce mesotheliomas than is needed to induce sarcomas (Sanders 1973). An increase in the incidence of mammary tumors was observed in rats given 3.6×10^{6} pCi (1.3×10^{5} Bq) plutonium-238 dioxide/kg (Sanders 1974).

2.3 TOXICOKINETICS

In radiation biology the term dose has a specific meaning. Dose refers to the amount of radiation absorbed by the organ or tissue of interest and is expressed in rads (grays). For example, estimation of this radiation dose to lung tissue or specific cells in the lung from a given exposure to plutonium is accomplished by modeling the sequence of events involved in the inhalation, deposition, clearance, and decay of

plutonium within the lung. While based on the current understanding of lung morphometry and experimental data on plutonium toxicokinetics, different models make different assumptions about these processes, thereby resulting in different estimates of dose and risk. Other models estimate dose from ingestion of plutonium. These models are described in numerous reports including Bair (1985), EPA (1988), ICRP (19783, James (1988), and NEA/OECD (1983). In this section the toxicokinetics of plutonium is described based on the available experimental data rather than on descriptions derived from models.

2.3.1 Absorption

2.3.1.1 Inhalation Exposure

The most common route of exposure to plutonium is inhalation. The absorption of plutonium following inhalation was dependent on its physicochemical properties including isotope number, the mass deposited, valence, chemical compound, and particle size (Bair et al. 1962b; Guilmette et al. 1984). Depending on the plutonium compound, it may be either soluble or insoluble. Plutonium as the citrate or nitrate was more soluble than the dioxide compound. Plutonium dioxides prepared at temperatures of 700°C or higher had a slower absorption rate compared to air-oxidized forms (Sanders and Mahaffey 1979). The absorption of plutonium was also dependent upon its respirable fraction, or that fraction of the total concentration of plutonium which may deposit in the nonciliated part of the lung. The respirable fraction of plutonium is composed of particles less than 10 pm Activity Median Aerodynamic-Diameter (AMAD), which indicates that only particles less than 10 pm AMAD would be retained in the nonciliated part of the lung and would be available for absorption (NEA/OECD 1981; Volchok et al. 1974).

The more soluble the form of plutonium, the more rapidly and extensively it was absorbed by the lungs (Ballou et al. 1972; Dagle et al. 1985). The insoluble forms of plutonium were absorbed from the lungs very slowly (Bair et al. 1962b; Bair and Willard 1962; Guilmette et al. 1984; Park et al. 1985) with the majority being deposited in the tracheobronchial region and then removed by the mucociliary apparatus. Insoluble particles may be engulfed by macrophages and alveolar cells (Metivier et al. 1980a; Sanders and Adee 1970) and taken up into the reticuloendothelial system (Leggett 1985).

Plutonium-238 administered as the soluble nitrate or as the less soluble dioxide form to dogs was absorbed from the lungs more rapidly than the corresponding forms of plutonium-239, possibly due to the lower mass of plutonium-238 (Da,gle et al. 1983; Park et al. 1972) or more likely, due to the higher specific activity of plutonium-238. However, when plutonium-239 nitrate was administered to rats, it was absorbed more readily than the plutonium-238 nitrate (Morin et al. 1972).

2.3.1.2 Oral Exposure

Absorption of plutonium from the gastrointestinal tract was minima and was dependent on age, chemical properties, stomach content. dietar? iron intake, and nutritional factors (Bomford and Harrison 1986; Harrison et al. 1986; Stather et al. 1980; Sullivan and Ruemmler 1988; Sullivan et al. 1983; Weeks et al. 1956). Oxidation state, administration media, extent of polymer formation, rate of hydrolysis, and mass administered did not appear to effect the absorption of plutonium (Carritt et al. 1947; Harrison and David 1987; Larsen et al. 198i; Stather et al. 1980, 1981).

Absorption of plutonium was slightly increased when administered in a citrate or nitrate solution and when administered as a very acidic solution (Weeks et al. 1956). Absorption of 0.003 to 0.01% of the administered plutonium citrate or nitrate has been reported in rats and hamsters (Carritt et al. 1947; David and Harrison 1984; Katz et al. 1955; Stather et al. 1981).

The absorption of plutonium after oral administration was age-related in laboratory animals. From 3 to 6% of administered plutonium may be absorbed by neonatal rats, hamsters, guinea pigs, and dogs (Cristy and Leggett 1986). A rapid decrease in absorption has been seen with increasing age. In hamsters between 1 day and 30 days of age, absorption of plutonium decreased from 3.5 to 0.003% of the administered dose (David and Harrison 1984).

Gastrointestinal absorption increased when plutonium was administered on an empty stomach. In hamsters that had been fasted for 8 to 24 hours, absorption increased to 0.1 to 0.15% of the administered plutonium citrate or ascorbate compared to 0.01% in animals which had not been fasted (Harrison et al. 1986).

Absorption of plutonium from the gastrointestinal tract was dependent on iron status. A four-fold increase in plutonium absorption occurred in rats that were iron deficient compared to those with normal iron status (Ragan 1977; Sullivan et al. 1986). Absorption of plutonium in nursing neonates of iron deficient dams was twice as much as neonates of iron-replete dams (Sullivan et al. 1986).

2.3.1.3 Dermal Exposure

The absorption of plutonium following dermal exposure was very limited. The amount absorbed depended on the thickness of the skin, the area of the skin exposed, the mass applied, the integrity of the skin, and the solution in which the plutonium is dissolved. Plutonium absorption through the intact palmar skin of a human was found to be less than 0.0002%/hr when administered as the nitrate in a 0.4N nitric acid solution (Langham 1959). Plutonium has been found to migrate down

hair follicles (Weeks and Oakley 1955) and into sweat and sebaceous glands (Buldakov et al. 1970).

2.3.1.4 Other Routes of Exposure

The absorption of plutonium after exposure was dependent on the route of administration. Intravenous injection delivered plutonium directly into the blood stream where it may then distribute in the body. Injection of plutonium into the peritoneal cavity (Sanders 1975a; Sanders and Jackson 1972) or into the muscle (Nenot et al. 1972) resulted in phagocytosis of particles which then enter the blood stream through the lymphatics. Intramuscular injection of plutonium-238 citrate to monkeys resulted in absorption of 95% of the administered dose from the site of injection in 10 days (Durbin et al. 1985). Absorption of plutonium after intraperitoneal injection was dependent on iron status. A two-fold increase in plutonium absorption occurred in rats which were iron-deficient compared .to those with normal iron status (Ragan 1977).

Absorption of plutonium through wounds has occurred in humans occupationally exposed (Hammond and Putzier 1964). Experiments in animals where plutonium-239 as the nitrate or dioxide was injected under the skin have been conducted to simulate this exposure. From these studies it has been found that about 80% of the administered plutonium nitrate or dioxide was absorbed (Dagle et al. 1984).

2.3.2 Distribution

2.3.2.1 Inhalation Exposure

The distribution of plutonium following absorption from the lungs was dependent on the physicochemical form deposited. In general, plutonium was distributed to the skeleton, liver, and lymph nodes; however, some plutonium has been found in all tissues. Information from humans who have been occupationally exposed to plutonium indicated that the highest concentrations of the absorbed plutonium were found in the tracheal-bronchial lymph nodes, followed by the liver, skeleton, and kidneys (Lagerquist et al. 1973). However, a more recent study by McInroy et al. (1989) reports that plutonium deposition in a small number of former nuclear industry workers was greatest, exclusive of the respiratory tract, in the skeleton followed by the liver, striated muscle, and other organs and tissues. These authors suggested that muscle and other soft tissues may act as a long-term storage depot for plutonium. Results from studies in laboratory animals indicated that absorption of the more soluble forms of plutonium led to greater distribution in the skeleton and liver (Dagle et al. 1985; Morin et al. 1972), while the less soluble dioxide form was distributed to a greater extent to the trachea-bronchial lymph nodes and the liver (Bair et al.

1966; Park et al. 1972). Distribution to the bone was greater with plutonium-238 nitrate than with plutonium-239 (Morin et al. 1972) and with the air-oxidized form of both plutonium-238 and plutonium-239 compared to the high-fired form (Sanders and Mahaffey 1979).

Particle size did not appear to affect distribution to the liver and skeleton in dogs (Guilmette et al. 1984). An age-related effect on distribution to the bone was reported by Guilmette et al. (1986). In immature dogs, a five-fold increase in distribution to the bone was seen compared to that in young adult dogs. Most information available on the distribution of plutonium following inhalation exposure is from studies where plutonium-239 dioxide was administered in a single dose to dogs. Additional information is also available on other chemical compounds, and isotopes in rodent species (Buldakov et al. 1972; Nenot et al. 1972; Sanders 1973b; Sanders et al. 1977).

The distribution of plutonium within the lungs after inhalation exposure was also dependent on several variables. In rats a more uniform exposure of lung cells occurred from administration of the air-oxidized form compared to the high-fired form (Sanders and Mahaffey 1979). Initially after exposure to the dioxide form, distribution in the lungs of hamsters was random with particles becoming more clumped with time (Diel et al. 1981).

The distribution of plutonium in the liver differed between the nitrate and dioxide forms. Administration of the nitrate form to dogs resulted in diffusely distributed activity found as single tracks, while administration of the dioxide form resulted in localized activity found as "alpha stars" with radioautography (Dagle et al. 1985).

2.3.2.2 Oral Exposure

In rats and dogs following absorption of plutonium from the gastrointestinal tract, up to 95% of the absorbed dose has been found to be distributed to the skeleton (Carritt et al. 1947; Larsen et al. 1981; Toohey et al. 1984). Plutonium was also distributed to a less extent to the liver, carcass, and soft tissues (Carritt et al. 1947; Katz et al. 1955; Larsen et al. 1981; Sullivan et al. 1984). The distribution of plutonium-237 in a bicarbonate solution administered via a gelatin capsule was greatest to the axial skeleton (Toohey et al. 1984).

2.3.2.3 Dermal Exposure

At early times after dermal exposure of rabbits to plutonium-239 nitrate, activity in blood was uniformly distributed, but later changed to a nonuniform distribution (Khodyreva 1966). Distribution of plutonium was greatest to the skeleton followed by muscle tissue, liver, kidney, spleen, heart, and lungs (Khodyreva 1966). In an earlier study in rats, the absorption of plutonium through intact skin did not appear

to result in distribution to the liver as compared to absorption through skin damaged by punctures or wounds where deposition in the liver was seen (Oakley and Thompson 1956).

2.3.2.4 Other Routes of Exposure

The distribution of plutonium was studied in terminally ill patients who had been given an intravenous injection of plutonium (Langham et al. 1980). Blood concentrations decreased rapidly (0.3% remained in the blood after 30 days). At death, which occurred from 16 to 450 days after injection, an average of 56% of the administered plutonium was in the bone marrow and on bone surfaces, while 23% was in the liver (Langham et al. 1980).

Although exposure by injection routes in humans is not likely, data from distribution studies in laboratory animals provides insight into the toxicokinetics of plutonium in the body. In dogs, once plutonium entered the blood stream, it was bound to transferrin, a serum transport protein (Stevens et al. 1968). Plutonium competed with iron for the transferrin in the blood. If transferrin was saturated with iron, then more plutonium would deposit in the liver and not in the bone (Ragan 1977). Similar binding of plutonium to transferrin was observed in human blood serum (Stover et al. 1968a).

In laboratory animals that received plutonium by intravenous injection, most plutonium was deposited in the liver and skeleton. No differences in distribution between plutonium-238 and plutonium-239 were reported in mice (Andreozzi et al. 1983); however, Ballou et al. (1967) reported that in rats deposition in the liver and other soft tissues was twice as great after intravenous administration of plutonium-239 than after administration of plutonium-238. In dogs, the concentration of plutonium polymer decreased in the lungs, spleen, and liver with time and increased in the skeleton and kidney (Stevens et al. 1976).

The distribution of plutonium after intravenous injection was age-dependent. The distribution of different chemical forms of administered plutonium did not differ in neonates, and activity was more uniformly distributed than in weanlings and adults (Mahlum and Sikov 1974; Sikov and Mahlum 1976). In immature dogs, increased deposition of plutonium was associated with bones that were undergoing active growth (Bruenger et al. 1978). The concentration of plutonium in the skull of neonates was twice as great as that in young adults, but distribution to the liver was not as great in neonates as in other age groups (Bruenger et al. 1978). Age at time of injection influenced distribution between the skeleton and the liver (Bruenger et al. 1980; Lloyd et al. 1978a, 1978b). In rats plutonium distribution within bone was different in weanlings compared to adults. In weanlings, there was a tendency for localization on periosteal surfaces and plutonium was seen in compact bone at earlier times (Sikov and Mahlum 1976).

In dogs and mice administered plutonium-239 as the citrate or as the polymer by intravenous injection, 15 to 31% or 55 to 70%, respectively, of the injected dose was distributed to the liver after 6 days (Baxter et al. 1973; Stover et al. 1959). In rats at 30 days post-exposure to plutonium as the citrate or as the polymer, 9.6 or 40%: respectively, was distributed to the liver (Carritt et al. 1947). The distribution of activity in the liver was uniform following administration of the citrate and nonuniform after administration of the polymer (Baxter et al. 1973; Brooks et al. 1983; Cochran et al. 1962).

The percent of plutonium-239, administered by intravenous injection as the citrate or as the polymer, that distributed to the skeleton of dogs and mice was 2.8 to 3.1% or 0.1 to 0.2%, respectively, after 6 days (Baxter et al. 1973). In rats 30 days after exposure to plutonium-239 as the citrate or as the polymer, 56.9 or 29.4%, respectively, distributed to the bone (Carritt et al. 1947). In dogs plutonium distribution in the skeleton was greatest to the trabecular or "spongy" bone and more was found in the red bone marrow, which is perfused with blood, compared with yellow or fatty bone marrow (Smith et al. 1984; Wronski et al. 1980). The rate of deposition in bone may be related to the rate of blood flow to bone, and in mice there appears to be a threshold rate for blood flow below which plutonium will not deposit to bone (Humphreys et al. 1982).

A small fraction of the plutonium taken in has been found to distribute to the gonads of mice following intravenous exposure. In mice exposed to plutonium-239 citrate, about 0.02 to 0.06% of the administered dose was distributed to the testes (Andreozzi et al. 1983; Ash and Parker 1978; Green et al. 1976). In the testes, plutonium was associated with the interstitial tissue (Ash and Parker 1978; Brooks et al. 1979; Green et al. 1976). Plutonium has also been measured in the ovarian tissue of mice exposed to plutonium-239 citrate (Green et al. 1977).

Plutonium-239 citrate has been shown to cross the placental membrane and has been found in the fetus in both mice and baboons following intravenous injection (Green et al. 1979; Sikov et al. 1978b; Weiss and Walburg 1978). The fractional placental transfer of plutonium citrate was found to be inversely proportional to the administered dose (Weiss and Walburg 1978). The greatest amounts of plutonium were found in the fetal membranes followed by the placenta and then the fetus (Sikov et al. 1978b). Plutonium was distributed to the gastrointestinal tract, liver, and mineralized areas of the bone in the fetus (Green et al. 1979).

After the absorption of plutonium from a wound site, it may be absorbed in the blood stream and distributed to the regional lymph nodes, liver, spleen, skeleton, and other tissues. In dogs exposure to plutonium dioxide through a wound resulted in greater distribution to

the lymph nodes and less to the skeleton as compared with exposure to plutonium nitrate (Dagle et al. 1984). Distribution to the spleen of dogs exposed to the dioxide form was greater than to the skeleton, while distribution to the spleen of dogs exposed to the nitrate form was less than to the skeleton. Comparable amounts of both forms were distributed to the liver and the skeleton (Dagle et al. 1984).

2.3.3 Metabolism

Plutonium occurs naturally in several valence states. but in the body the most common state is (IV) due to stabilization by ligands and complexing agents (ICRP 1972). Plutonium does not esist as a simple ion at physiological pH and, therefore, tends to hydrolyze and form polymers. The tendency for plutonium to hydrolyze should increase with increasing atomic number because the hydrolytic behavior is determined by ionic charge and size (ICRP 1972). When plutonium is complexed with citrate, it is less likely to form polymers and remains more soluble in the body.

2.3.4 Excretion

2.3.4.1 Inhalation Exposure

Elimination of plutonium following exposure by inhalation appears to be dependent upon the form of plutonium and may vary among species. After inhaiation exposure to plutonium, the clearance pattern from the lungs appeared to be biphasic. In rats, the half-time for clearance of plutonium-238 or -239 dioxide from the lungs for the first phase was from 20 to 30 days and for the second phase was from 180 to 250 days (Sanders et al. 1976, 1977, 1986). In the first phase, 70 to 76% of the plutonium was removed with the remainder of that excreted removed in the second phase. Retention of plutonium in the body after it translocates to other tissues may be very long. In dogs exposed to plutonium-239 dioxide, 85% of the administered amount was retained in the body 9 to 10 years after exposure (Park et al. 1972). Retention of plutonium dioxide in the lungs of dogs was not constant over time, which may be related to an increased rate of solubilization of the particles with time, resulting in greater translocation to other organs (Hahn et al. 1981). The retention half-time increased with increasing particle size (Bair et al. 1962b; Guilmette et al. 1984). The retention half-time for the plutonium-239 isotope was greater than for the plutonium-238 isotope (Park et al. 1972). With repeated exposure to plutonium-239 dioxide, it appeared that each administered amount was retained independently with its own retention characteristics (Die1 and Lundgren 1982).

The excretion of plutonium by humans approximately 30 years after occupational exposure to plutonium particles, primarily by inhalation, appeared to indicate that more plutonium was cleared in the urine than in the feces (Voelz et al. 1979). However, Leggett (1985) stated that,

at equilibrium, 4 times more plutonium was eliminated in the feces than in the urine. In laboratory animals, the primary route of excretion of plutonium was reportedly through the feces. From 10 to 35 times more plutonium was excreted in the feces than in the urine in dogs and rats (Bair and McClanahan 1961; Die1 and Lundgren 1982; Sanders et al. 1976, 1977). In rats exposed by inhalation or intramuscular injection, greater amounts of plutonium have been found in the feces as soon as 6 days following inhalation exposure. This may be due to the removal of particles from the respiratory tract by the mucociliary elevator and the consequent swallowing of these particles or due to biliary clearance (Morin et al. 1972).

2.3.4.2 Oral Exposure

Most of plutonium administered to dogs in a bicarbonate solution by the oral route was eliminated in the feces, with an average excretion of 98% of the administered dose after 5 or 6 weeks (Toohey et al. 1984). In mice and rats total retention of plutonium varied from 0.17 to 0.24% of the administered activity and was not dependent on oxidation state or on the medium in which it was administered (Larsen et al. 1981). Retention in the liver of mice and rats was 0.036 and 0.054%, respectively, of the initial dose (Larsen et al. 1981) and in the skeleton plus liver of fasted dogs was 0.063% of the administered dose (Toohey et al. 1984).

Retention of plutonium in rat neonates was 100 times greater than in adults (Sullivan et al. 1984). More plutonium was found in the wall of the small intestine than in the walls of the stomach and large intestine of rats (Fritsch et al. 1988).

2.3.4.3 Dermal Exposure

No studies were located regarding excretion in humans or laboratory animals after dermal exposure to plutonium.

2.3.4.4 Other Routes of Exposure

Little information is known about the excretion of plutonium in humans after exposure through other routes. From terminally ill humans who were administered an intravenous injection of plutonium it appeared that the major route of elimination was in the urine (Langham et al. 1980). The biological half-time in these individuals was estimated to be 118 years and the retention half-time in the liver was estimated to be greater than 1 year. Data from humans occupationally exposed through wounds indicated that excretion patterns could net be predicted following this type of exposure (Hammond and Putzier 1964).

From injection studies in laboratory animals it was found that retention was dependent on the isotope, chemical form, and sex. In dogs

plutonium-239 was retained longer than plutonium-237 (Bair et al. 1974). The retention of plutonium-242 and plutonium-244 was similar, and was longer than the retention time for plutonium-236 and piutonium-239 (Guilmette et al. 1978). In mice no difference was seen in fractional retention at low and high doses (Andreozzi et al. 1983). In hamsters more plutonium administered intravenously in an insoluble form (plutonium dioxide) was retained than plutonium administered in a soluble form (plutonium citrate) (Brooks et al. 1976b). Retention after intraperitoneal injection of mice and hamsters may be sex-dependent; females retained more in the liver than males (Smith et al. 1576, 1978). However, retention after intravenous injection was not sex-dependent (Smith et al. 1978). Total retention and liver retention increased with age (Bruenger et al. 1980; David and Harrison 1984).

The whole body retention of intravenously administered plutonium-237 and/or -239 citrate in dogs varied from approximately 85% to almost 100% (Bair et al. 1974; Lloyd et al. 1976, 1984) with liver retention of about 25% (Bair et al. 1974; Lloyd et al. 1976, 1984; Stover et al. 1962) and skeietal retention of about 50% (Bruenger et al. 1980; Lloyd et al. 1978a, 1978b, 1984). Liver retention was found to be dosedependent (Stover et al. 1962). In hamsters, the whole body retention of plutonium-239 dioxide was approximately 100% (Brooks et al. 1983). Plutonium was found to be retained for an indefinite time in the testes and ovaries of mice and rats (Green et al. 1977; Miller et al. 1989; Taylor 1977). Retention at the site of administration after exposure which simulated wounds was from 16 to 21% of the administered dose (Dagle et al. 1984).

The half-life for removal of plutonium was very long. In mice the biological half-life of plutonium-238 or 239 citrate in the skeleton was one to two times the animal's lifespan and in the liver the half-life was 350 days (Andreozzi et al. 1983). In dogs the half-life of plutonium-239 citrate in the liver was 3,081 days, in the spleen was 995 days, and in the kidney was 1,520 days (Stover et al. 1968b). A long effective half-life has been reported in hamsters with 85% of injected plutonium-239 citrate still in the bone and liver 700 days after administration (Benjamin et al. 1976).

In mice plutonium-239 administered as a polymer in a non-citrate solution was cleared from the blood rapidly, 99% in 15 minutes, while only 20% of plutonium administered as a monomer in a citrate solution was cleared in the same time (Baxter et al. 1973). Most plutonium was retained in the body, and the remainder was excreted. In mice, hamsters, and dogs from 10 to 30% of plutonium was excreted primarily in feces (Baxter et al. 1973,; Brooks et al. 1983; Lloyd et al. 1976, 1978b, 1984). Plutonium was also shown to be removed from the body through lactation; however, the amount of plutonium in milk was not reported (Taylor 1980). In nursing rats administered plutonium-239 citrate, the total body burden was decreased 10% by lactation (Taylor 1980).

2.4 RELEVANCE TO PUBLIC HEALTH

Plutonium isotopes are products of neutron absorption processes in nuclear reactors generated by nuclear processes. Exposure to plutonium in environmental media poses the potential for causing adverse health effects. Plutonium and other alpha-emitting radionuclides (ATSDR 1990) exert their biological effects after entering the body and depositing in radiosensitive tissues. Inhalation is the primary route of plutonium exposure for humans in either occupational or environmental settings. Translocation from the lungs to other organs in the body depends on a variety of factors including the solubility of the plutonium compound and the particular plutonium complex. Plutonium is not readily absorbed from the gastrointestinal tract or through intact skin.

Plutonium emits ionizing radiation primarily in the form of alpha particles. The type and severity of the biological response to this radiation will depend not only on the amount of radiation emitted but also on the radiosensitivity of the tissue and contact (retention) time. In general, tissues undergoing rapid cell regeneration are more radiosensitive than slower or nonregenerating cell systems (see Appendix B).

Animal studies have demonstrated that exposure to high radiation doses of plutonium isotopes have resulted in decreases in lifespan, diseases of the respiratory tract, and cancer. The target tissues appear to be the lungs and associated lymph nodes, the liver, and bones. However, these observations in animals have not been corroborated by epidemiological investigations in humans exposed to smaller amounts of plutonium.

Death. No deaths in humans specifically associated with plutonium have been reported following acute plutonium exposure. Epidemiological studies of occupational cohorts did not report any increases in deaths due to nonmalignant diseases. However, the highest radiation levels reported in workers were 100- to 1,000-fold lower than the radiation levels that resulted in death (due to respiratory failure) in some laboratory animals. Acute exposures to high levels of plutonium isotopes, administered as dioxides, citrates, or nitrates, were fatal to several laboratory species when exposure occurred by the inhalation, oral, or injection routes. Survival time was radiation dose-related for all of these routes of exposure. By the inhalation route in animals, nonmalignant respiratory disease was characterized by radiation pneumonitis, pulmonary fibrosis, alveolar edema, and occasionally hyperplasia and metaplasia with death occurring within weeks or months of the initial exposure to high concentrations. It is likely that mortality due to radiation-induced sickness, such as radiation pneumonitis, could occur in humans at sufficiently high radiation doses. Such amounts of radiation, however, would be expected to occur only with

an extremely large accidental release but not at the radiation levels attributable to plutonium currently identified in the ambient environment.

Respiratory Effects. Neither deaths due to respiratory disease nor reduced respiratory function have been reported among the occupationally exposed cohorts-. Respiratory diseases characterized by pneumonitis, fibrosis, edema, and respiratory dysfunction have been reported in all laboratory species tested following acute exposure to high concentrations of plutonium by the inhalation or injection routes. The severity of the respiratory disease and the time to death from respiratory disease correlated with the activity concentration. Induction of this type of respiratory disease in humans could occur at high exposure levels, which greatly exceed those commonly found in the environmental setting. However, the radiation dose that might result in either pulmonary dysfunction or pulmonary disease in humans has not been specifically identified. A no observed adverse effect level (NOAEL) was not established with certainty based on the data from animal studies. The types of adverse respiratory effects observed appear to be consistent with the pattern of alpha radiation damage that may occur in slower regenerating tissues such as the lungs (see Appendix B). That being the case, production of respiratory tissue damage in the lungs may occur but may not be immediately apparent, especially at low environmental exposures.

Hematological Effects. No acute hematological effects were observed among human volunteers given a single injection of plutonium, but no follow-up study was conducted to assess the possibility of delayed effects. No adverse hematological effects were reported among the various occupational cohorts who underwent medical examinations. There is considerable evidence from animal experiments that plutonium produces adverse effects in the hematopoietic system. Lymphopenia was the most common finding following inhalation exposure in animals, while anemia, bone marrow depression, and decreases in white blood cells and hematopoietic stem cells occurred following injection of plutonium in animals. The lymphopenia was dose-related and correlated both in magnitude and time of appearance post-exposure with the initial lung burden of inhaled plutonium. Hematological abnormalities have occurred in human populations following exposure to external radiation (i.e., gamma and high-energy beta), and blood-forming cells could be a target for internally deposited alpha radiation (see Appendix B); however, the relevance of the hematological effects seen in animals at high doses to potential health effects in humans environmentally exposed to plutonium is unclear.

Hepatic Effects. Adverse hepatic effects associated with plutonium exposure have not been reported in humans. There is evidence in animals that inhalation or injection of plutonium results in degenerative liver

injury and functional impairment of the liver. It is likely that these effects are directly related to the radiation toxicity of plutonium (since liver tumors have been observed), rather than a secondary response to other adverse biological events in the body, although the liver is expected to be less radiosensitive than more rapidly regenerating cells. Subtle changes in liver function as a result of low doses of plutonium have not been evaluated. It is unclear from the reported literature whether complete liver function tests were performed in the occupational cohorts under investigation. As with the other nonstochastic biological effects discussed, the level below which hepatic effects are unlikely to occur as not been clearly defined; therefore, the effects of plutonium on hepatic function and histology at levels encountered in the environment have not been identified.

Musculoskeletal Effects. Adverse musculoskeletal effects associated with plutonium exposure have not been reported in humans. There is limited evidence of noncancerous bone damage and no evidence of muscle damage in laboratory animals exposed to plutonium. Muscle tissue is considered to be relatively resistant to the effects of alpha radiation (see Appendix B); therefore, damage to muscle tissue is not expected in animals and should not be of concern to individuals exposed to plutonium in the environment. Bone damage occurred in animals given plutonium by the inhalation route and the injection route. The more soluble forms of plutonium resulted in bone damage when inhaled. Spontaneous fractures, which were age-dependent, along with atrophy and osteodystrophy, were seen at high radiation doses. These skeletal effects may be due to radiation damage to rapidly dividing osteoblasts especially in the ends of long bones; therefore, children could be a sensitive subpopulation and could be more sensitive to radiation-induced bone damage.

Gastrointestinal Effects. Adverse gastrointestinal effects associated with plutonium exposure have not been reported in humans. Gastrointestinal effects in animals have been reported only in an oral study in neonatal rats. Because the epithelial cells of neonatal rodents are immature and poorly enclosed, these cells may be more sensitive to radiation damage in the neonate than in the adult, so it is possible that infants would represent a sensitive subpopulation among people exposed to plutonium by the oral route. Gastrointestinal absorption is limited, and translocation to other organ systems is also limited. The probability of exposure of humans to plutonium by the oral route is expected to be small; however, if it were to occur, localized radiation damage to the epithelial cells of the stomach may occur.

Immunological Effects. Adverse immunological effects associated with plutonium exposure have not been reported in humans. Immunotoxicity has been observed in several species administered plutonium by inhalation and in dogs given plutonium by injection.

Plutonium is translocated from the lungs to the tracheobronchial and mediastinal lymph nodes, and has also been found in the hepatic lymph nodes. Immunotoxicity ranged from alterations in antibody-forming cells to atrophy and fibrosis of lymph glands. The animal data present a consistent view that plutonium affects immune function either by destruction of lymph nodes or circulating lymphocytes or other alterations in immune system competence. The implications of this for human health are unknown; however, it is possible that if alterations in immune system competence were to occur, then the ability to respond to other disease situations unrelated to plutonium could be affected. Tine immunotoxicity which occurred in laboratory animals was observed at concentrations lower than those that resulted in overt clinical (respiratory) effects. These findings suggest that individuals exposed to plutonium could develop subtle changes in the immune system that may reduce immune.competence at doses that may not induce overt signs of toxicity.

Genotoxic Effects. Tables 2-4 and 2-5 present the results of in vitro and in vivo genotoxicity studies, respectively. Epidemiological studies do not provide evidence that plutonium produces genetic damage in humans. In particular, the data from persons involved in the Manhattan project after a 30-year follow-up have been negative. In vitro tests using human lymphocytes irradiated with plutonium-238 or plutonium-239 demonstrated increases in sister chromatid exchange (Aghamohammadi et al. 1988) and chromosomal aberrations (Purrott et al. 1980), respectively. In vitro studies have also shown a dose-related linear increase in mutation frequencies at the hypoxanthine-guanine phosphoribosyl transferase locus in cultured human fibroblasts (Chen et al. 1984).

The animal in vivo and in vitro studies are in agreement. Plutonium induced chromosomal aberrations in several species in vivo and in the corresponding cell lines when cultured in vitro. Chromosomal aberrations (Welleweerd et al. 1984) and gene mutations (Thacker et al. 1982) were seen in Chinese hamster cells cultured in vitro. Plutonium was not genotoxic using the Ames test for mutagenicity in several strains of Salmonella typhimurium (Fritsch et al. 1980).

Cancer. Epidemiological studies of occupational cohorts with long-term exposure to plutonium include those of workers at Los Alamos National Laboratory, Rocky Flats Nuclear Weapons Plant, or Hanford Weapons Plant and the cohort involved in the original Manhattan project at Los Alamos. None of these studies has demonstrated an unequivocal association between exposure to plutonium and mortality from cancer at any anatomical location in workers after 30 or more years. These

TABLE 2-4. Genotoxicity of Plutonium In Vitro

End Point	Species/Test System	Result	Reference
Prokaryotic organisms:			
Gene mutation	Salmonella typhimurium/ TA-100, TA-98, TA-1535, TA-1537, TA-1538, TA-2420, TA-2421	-	Fritsch et al. 1980
Mammalian cells:			
Gene mutation	Chinese hamster/ovary cell line	+	Fritsch et al. 1980
Chromosomal aberrations	Human/lymphoblastic cell line	+	Fritsch et al. 1980
	Human/lymphocytes	+	Purrott et al. 1980
	Chinese hamster/M3-1 cells	+	Welleweerd et al. 1984
Gene mutation	Human/embryonic skin fibroblasts	+	Chen et al. 1984
	Chinese hamster/ovary cell line	+	Barnhart and Cox 1979
	Chinese hamster/V79-4 cells	+	Thacker et al. 1982
DNA damage	Chinese hamster/V79-379A cells	+	Prise et al. 1987
Reduction in radio-resistance	Mouse-rat/hybrid cell line	+	Robertson and Raju 1980
Sister chromatid exchanges	Human/lymphocytes	+	Aghamohammadi et al. 1988

- = negative result
+ = positive result

TABLE 2-5. Genotoxicity of Plutonium In Vivo

End Point	Species/Test System	Result	Reference
Mammalian systems:			
Chromosomal aberrations	Chinese hamster/testes	-	Brooks et al. 1979
	Mouse/testes	+	Brooks et al. 1979; Beechey et al. 1975
	Chinese hamster/liver cells	+	Benjamin et al. 1976; Brooks et al. 1976b
	Mouse/bone-marrow cells	+	Svoboda et al. 1987
	Syrian hamster/lung cells	+	Stroud 1977
	Chinese hamster/blood cells	+	Brooks et al. 1976a
	Human/peripheral lymphocytes	(+)	Brandon et al. 1979; Tawn et al. 1985
	Human/whole blood	-	Hempelmann et al. 1973; Voelz et al. 1979
	Human/blood lymphcytes	+	Schofield et al. 1980
	Monkey/blood lyphocytes	+	LaBauve et al. 1980
Dominant lethal	Mouse/germ cells	-	Searle et al. 1976
	Mouse/germ cells	+	Lüning et al. 1976a, 1976b
	Mouse/ovaries	(+)	Searle et al. 1982
Reciprocal/ chromosome translocation	Mouse/spermatogonia	+	Beechey et al. 1975; Generoso et al. 1985
		-	Searle et al. 1976

+ = positive result
- = negative result
(+) = positive or marginal result

studies have one or more of the same limitations inherent in other epidemiological studies. These include small cohort size, poorly defined exposure information, or insufficient follow-up periods. However, the Rocky Flats study was extensive and exposures were documented from health physics records. One limitation of the Rocky Flats study is that the worker cohort was divided into only two exposure categories based on body burden, less than or greater than 2,000 pCi (74 Bq) plutonium. The authors concluded that the study suggested an increased risk of lymphopoietic cancers based on a total of four such lymphopoietic neoplasms, one each of lymphosarcoma/reticulosarcoma, non-Hodgkin's lymphoma, multiple myeloma and myeloid leukemia. However, no elevated cancer incidences were noted in tissues with the highest concentrations of plutonium (tracheobronchial lymph nodes, lungs, liver, and bone) as demonstrated in autopsy samples.

In contrast, the results from numerous animal studies are conclusive. Plutonium at the concentrations administered produced lung, liver, and bone cancers primarily when administered by the inhalation or injection routes in dogs, mice, rats, and nonhuman primates. Only Syrian hamsters appeared to be resistant to plutonium-induced tumors, even though hamsters developed the same nonmalignant respiratory effects. The current understanding of radiation-induced carcinogenesis is that it is a stochastic process, that is, one without a threshold for developing cancer. Mechanistically, plutonium should be considered to have the potential to cause cancer due to the emission of alpha particles (ATSDR 1990). While it is true that cancer in animals resulted from extremely large concentrations that are orders of magnitude higher than any occupational or environmental exposure (except under an accident scenario), it is appropriate and health protective to assume that some level of risk of cancer exists from exposure of humans to plutonium.

2.5 BIOMARXERS OF EXPOSURE AND EFFECT

Biomarkers are broadly defined as indicators signaling events in biologic systems or samples. They have been classified as markers of exposure, markers of effect, and markers of susceptibility (NAS/NRC 1989).

A biomarker of exposure is a xenobiotic substance or its metabolite(s) or the product of an interaction between a xenobiotic agent and some target molecule or cell that is measured within a compartment of an organism (NAS/NRC 1989). The preferred biomarkers of exposure are generally the substance itself or substance-specific metabolites in readily obtainable body fluid or excreta. However, several factors can confound the use and interpretation of biomarkers of exposure. The body burden of a substance may be the result of exposures from more than one source. The substance being measured may be a metabolite of another xenobiotic (e.g., high urinary levels of phenol

can result from exposure to several different aromatic compounds). Depending on the properties of the substance (e.g., biologic half-life) and environmental conditions (e.g., duration and route of exposure), the substance and all of its metabolites may have left the body by the time biologic samples can be taken. It may be difficult to identify individuals exposed to hazardous substances that are commonly found in body tissues and fluids (e.g., essential mineral nutrients such as copper, zinc and selenium). Biomarkers of exposure to plutonium are discussed in Section 2.5.1.

Biomarkers of effect are defined as any measurable biochemical, physiologic, or other alteration within an organism that, depending on magnitude, can be recognized as an established or potential health impairment or disease (NAS/NRC 1989). This definition encompasses biochemical or cellular signals of tissue dysfunction (e.g., increased liver enzyme activity or pathologic changes in female genital epithelium cells), as well as physiologic signs of dysfunction such as increased blood pressure or decreased lung capacity. Note that these markers are often not substance specific. They also may not be directly adverse, but can indicate potential health impairment (e.g., DNA adducts). Biomarkers of effects caused by plutonium are discussed in Section 2.5.2.

A biomarker of susceptibility is an indicator of an inherent or acquired limitation of an organism's ability to respond to the challenge of exposure to a specific xenobiotic. It can be an intrinsic genetic or other characteristic or a preexisting disease that results in an increase in absorbed dose, biologically effective dose, or target tissue response. If biomarkers of susceptibility exist, they are discussed in Section 2.7, "POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE."

2.5.1 Biomarkers Used to Identify or Quantify Exposure to Plutonium

Biomarkers of exposure to plutonium include the presence of plutonium in urine, which is identified by measuring alpha activity. From the levels of radioactivity in the urine, body burdens of plutonium may be estimated by the use of models. Body burdens of plutonium in several populations, including workers at Los Alamos National Laboratory, the Rocky Flats facility, and the Hanford facility, have been estimated from urinalysis data. However, whole body burdens determined from selected tissues obtained at autopsy have generally been lower than those estimated from urinalysis data (Voelz et al. 1979). The presence of radioactivity from plutonium in urine is specific to plutonium exposure. Plutonium may be found in the urine after any exposure duration (e.g., acute, intermediate, chronic). Although it can be assumed that exposure to greater levels of plutonium would result in the presence of greater levels of radioactivity in the urine, no information was located to directly quantify this relationship.

2.5.2 Biomarkers Used to Characterize Effects Caused by Plutonium

Limited information is available regarding biomarkers of effect of plutonium exposure. The presence of chromosome aberrations has been reported in laboratory animals following exposure to plutonium. Chromosome aberrations have also been reported in humans following exposure through open wounds, but evidence from epidemiologic studies where exposure occurred via inhalation have been equivocal (Brandom et al. 1979; Hempeimann et al. 1975; Tawn et al. 1985: Voelz et al. 1979). Although the presence of chromosome aberrations could be considered a biomarker of effect, the number of chemicals that could cause this effect is so great that the effect would not be considered plutoniumspecific. In dogs, the earliest observed biological effect of exposure to plutonium is a dose-related lymphopenia that correlated in magnitude and time of appearance post-exposure with initial lung burden (Park et al. 1988; Ragan et al. 1986). Although there is currently no information in humans regarding the occurrence of this effect, the presence of lymphopenia in humans following plutonium exposure might be a potential biomarker of effect.

Biomarkers of effect for plutonium exposure may exist but were not located in the reviewed literature. For more information on biomarkers of effects for the immune, renal, and hepatic systems see ATSDR/CDC Subcommittee Report on Biological Indicators of Organ Damage (1990) and for biomarkers of effect for the neurological system see OTA (1990). For more information on health effects following exposure to plutonium see Section 2.2.

2.6 INTERACTIONS WITH OTHER CHEMICALS

The toxicokinetics of plutonium appear to be influenced by exposure to cigarette smoke. Cigarette smoke, when administered to mice following inhalation exposure to plutonium-239 dioxide, appeared to inhibit the clearance of plutonium (Talbot et al. 1987). At 49 days post-exposure, animals exposed to plutonium and cigarette smoke retained approximately 20% more plutonium than those animals exposed to plutonium alone.

Exposure to inhaled plutonium-239 dioxide followed by intratracheal instillation of benzo(a)pyrene resulted in a higher incidence of lung tumors and a decrease in median survival time compared to animals exposed to plutonium-239 dioxide alone (Metivier et al. 1984). As the dose of benzo(a)pyrene increased, survival time decreased. Exposure of rats to a single intra-abdominal injection of a mixture of plutonium-239 dioxide and benzo(a)pyrene resulted in an additive effect in the induction of abdominal sarcomas, compared to animals given benzo(a)pyrene or plutonium only (Sanders 1973a).

A decrease in median survival time was observed in rats injected intravenously with plutonium-239, immediately followed by exposure to Xrays (Ballou et al. 1962), as compared to those animals exposed to plutonium alone. As exposure to X-rays increased, survival time decreased. However, when exposure to X-ray was delayed (as much as 1S days) following exposure of the rats to plutonium-239, the number of deaths occurring before 40 days was reduced.

Exposure of rats to plutonium-239 dioxide and asbestos by intraperitoneal injection resulted in a higher incidence of abdominal tumors compared to animals exposed to plutonium-239 dioxide alone (Sanders 1973a). However, this additive effect of asbestos and plutonium was not observed in the induction of pulmonary sarcomas when asbestos was administered to rats in combination with plutonium-239 oxide via intratracheal instillation (Sanders 1975b). In the same study, asbestos did not influence the translocation of plutonium in rats. However, asbestos increased the pulmonary retention of plutonium compared to those exposed to plutonium only (Sanders 1975b).

An increased incidence of metaplasia was observed in rats exposed via inhalation to a single exposure of plutonium-239 dioxide followed by administration of 1 or 10 mg vitamin C/ml of drinking water for 1 year post-exposure, compared to those animals exposed to plutonium only (Sanders and Mahaffey 1963). However, the incidence of squamous cell carcinomas in admals exposed to plutonium and vitamin C decreased with increasing dose of vitamin C. The authors state that vitamin C may interfere with the progression of squamous cell metaplasia to squamous cell carcinoma.

Studies in laboratory animals have also shown the influence of metals on the toxicokinetics of plutonium. Pretreatment of rats with a subcutaneous injection of cadmium or copper followed by an intravenous injection of plutonium-239 or plutonium-238 resulted in changes in the distribution patterns of plutonium, but not in total retention of either isotope. Plutonium retention of both isotopes, following pretreatment with either metal, was increased in the spleen and the kidneys, as compared to animals treated with plutonium only (Volf 1980). Copper pretreatment appeared to increase the retention of plutonium in the liver, while cadmium pretreatment appeared to decrease plutonium retention in the liver. These differences in retention of plutonium in the liver may reflect different properties of the respective metalbinding proteins or different mechanisms of action (Volf 1980).

Exposure of rats via inhalation to beryllium oxide followed by exposure to plutonium-239 oxide resulted in increased retention of plutonium in the lungs of rats and subsequently, increased translocation of plutonium to thoracic lymph nodes as compared to plutonium-treated, controls (Sanders et al. 1978). Although lung retention of plutonium was increased and beryllium and plutonium are both considered to be lung

carcinogens, combined exposures of beryllium and plutonium-239 did not significantly increase the incidence of lung tumors in rats, compared to rats treated with plutonium only (Sanders et al. 1978).

Administration of alcohol prior to exposure to plutonium appears to have an effect on the toxicokinetics of plutonium. Rats were treated orally with 12.5 or 25% ethanol (in 25% sucrose) for 1 or 6 weeks followed by an intravenous injection of polymeric plutonium-239 and were sacrificed 1 or 41 days post-exposure (Mahlum and Hess 1978). In animals given ethanol for 6 weeks, retention of plutonium in the liver was increased at 1 day post-exposure, but returned to normal 41 days post-exposure, compared to animals exposed to plutonium only. At 1 day post-exposure, lung retention of plutonium was increased in animals given ethanol for 1 week, while lung retention of plutonium was decreased in animals given ethanol for 6 weeks. These differences were still apparent at 41 days post-injection (Mahlum and Hess 1978).

Animal studies have been conducted to study the relative hazards of "diffuse" vs. "localized" irradiation of the lung (Anderson et al. 1979) to determine if there is a "hot particle" or "hot spot" effect. In these studies, hamsters were exposed by instillation or intravenous injection to plutonium-238 or -239 oxide contained in zirconium dioxide spheres. Following "localized" exposure, the incidence of lung tumors was significantly increased (3/102) only at the highest exposure [3.5×10^6 pCi (1.3×10^5 Bq) plutonium-238/kg body weight]. However, following "diffuse" exposure, a significant increase in the incidence of lung tumors was observed at exposures of 8.4×10^5 pCi (3.1×10^4 Bq) plutonium-238/kg body weight and 9.4×10^5 pCi (3.5×10^4 Bq) plutonium-239/kg body weight. The authors concluded that for a given lung burden of plutonium, the most hazardous distribution was "diffuse."

Animal studies have shown the effects of chelation therapy on the removal of previously incorporated actinide elements, such as plutonium. Exposure of young adult beagle dogs to a single intravenous injection of polymeric plutonium-239 plus plutonium-237 as a tracer, followed by weekly exposure to diethylenetriamine-pentaacetate (DTPA) as calcium salt (Ca-DTPA) or daily exposure of DTPA as zinc salt (Zn-DTPA), resulted in 14.6% or 10.4% plutonium-237 excretion, respectively, vs. 7.1% plutonium excretion at 24 hours post-exposure in those animals exposed to plutonium alone (Lloyd et al. 1978c). After 28 days, cumulative excretion (corrected for radioactive decay) reached 38.2% for Ca-DTPA, 49.4% for Zn-DTPA, and 12.1% for those animals treated with plutonium alone. The study indicated that daily exposure of beagle dogs to Zn-DTPA is more effective in increasing the excretion of incorporated plutonium than weekly exposure to Ca-DTPA. As speculated by the authors, the enhanced plutonium excretion may have occurred as a result of calcium replacement in Ca-DTPA or zinc replacement in Zn-DTPA by plutonium at the cellular level.

2.7 POPULATIONS THAT ARE UNUSUALLY SUSCEPTIBLE

Children may be particularly susceptible to the adverse effects of plutonium. Cells are replicating much faster in growing children than in adults. Rapidly regenerating cells are more radiosensitive than slowly regenerating cells (see Appendix B). Therefore, children may be more susceptible to the radiation effects of plutonium than adults.

Persons with chronic obstructive lung diseases may be more susceptible to the toxic effects of inhaled plutonium. Based on results from studies in rats with puimonary emphysema, plutonium deposition would be decreased in a person with pulmonary emphysema, but retention would be increased (Lundgren et al. 1981). Therefore, a greater radiation dose would be delivered to the lungs of a person with emphysema or other chronic obstructive lung diseases.

Persons who are anemic due to an iron deficiency may be more susceptible to the toxic effects of plutonium. Studies by Ragan (1977) have demonstrated that iron-deficient mice absorbed four times as much plutonium from the gastrointestinal tract as mice with normal iron levels. Therefore, persons who are iron deficient may absorb more plutonium (Sullivan and Ruemmler 1988).

2.8 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of plutonium is available. Where adequate information is not available, ATSDR, in conjunction with the National Toxicology Program (NTP), is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of plutonium.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

2.8.1 Existing Information on Health Effects of Plutonium

The existing data on health effects of inhalation, oral, and dermal exposure of humans and animals to plutonium are summarized in Figure 2-4. The purpose of this figure is to illustrate the existing information concerning the health effects of plutonium. Each dot in the figure indicates that one or more studies provide information associated with that particular effect. The dot does not imply anything about the

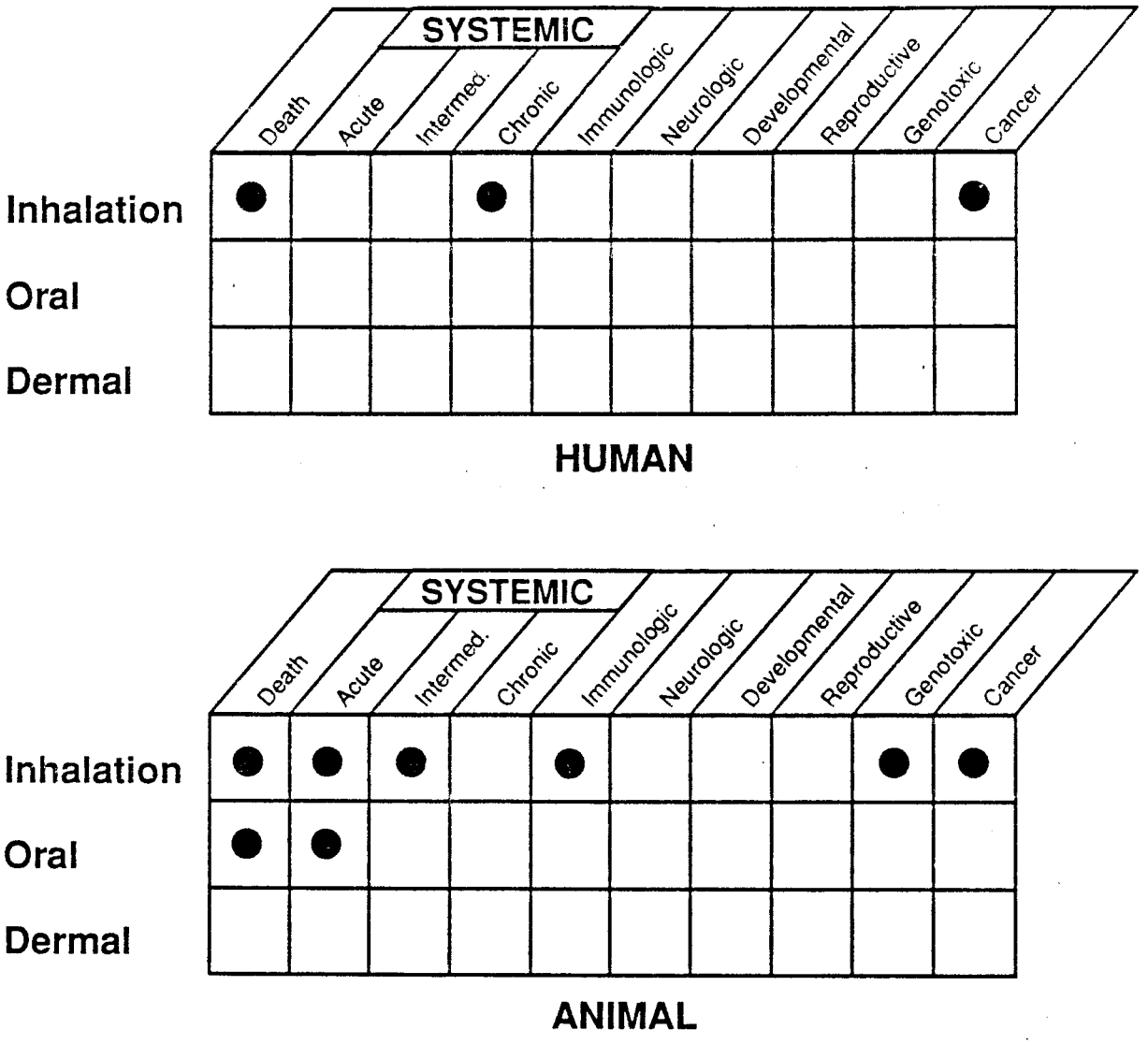

FIGURE 2-4. Existing Information on Health Effects of Plutonium

quality of the study or studies. Gaps in this figure should not be interpreted as "data needs" information.

Figure 2-4; graphically describes whether a particular health effect end point has been studied for a specific route and duration of exposure. Information on health effects in humans is very limited largely because exposed populations are small. Epidemiological studies of people who have been occupationally exposed by inhalation to plutonium have evaluated end points such as mortality, cancer, and systemic effects following chronic exposure. No information on health effects in humans after acute or intermediate exposure to plutonium was located. Information on health effects from animal studies is more extensive than that which has been reported in epidemiological studies. These studies in animals provide information on health effects following both acute and intermediate inhalation exposure and limited information on acute oral exposure.

2.8.2 Identification of Data Needs

Acute-Duration Exposure. The possibility of brief exposure of humans to plutonium exists at hazardous waste sites or at accidental spill sites. However, no data are available for humans exposed acutely via inhalation or oral routes. Information on the toxicity of plutonium in laboratory animals following single high-dose inhalation exposure is extensive and indicates that the lung is the main target organ for inhaled plutonium. Laboratory animals exposed by this route have developed pneumonitis, fibrosis, metaplasia, and cancer. Acute exposure of laboratory animals to lower doses of plutonium would be useful to identify possible inhalation toxicity in humans. Limited information on adverse effects in laboratory animals following acute oral exposure indicates that the gastrointestinal tract is the main target organ. However, kinetic studies indicate that plutonium absorbed from the gastrointestinal tract is distributed to the skeleton and other tissues; therefore, other organs may also be affected. Because there are no data on humans and animal data are insufficient, additional information is needed on adverse effects following acute exposure by the oral route. No data are available on adverse effects following acute dermal exposure in humans or animals. Limited information from kinetics studies in humans and animals indicates that there is little absorption of plutonium through intact skin. However, plutonium deposited in wounds is absorbed and distributes to numerous organs, including regional lymph nodes and the liver. Since industrial accidents resulting in plutoniumcontaminated wounds are known to occur, additional information on adverse effects following this type of exposure would be helpful. One outstanding problem with all of the existing acute exposure tests in laboratory animals is that the doses tested are extremely high. Further single-dose studies for all exposure routes using a number of lower

exposure concentrations would be useful in determining any dose-response relationship for adverse health effects.

Intermediate-Duration Exposure. Limited data from intermediate-Duration exposure studies in laboratory animals indicate that the lung is the target organ for inhaled plutonium. In one study, hamsters developed pneumonitis following intermittent exposure to plutonium. However, no data are available on effects of inhalation exposure for this duration in humans. Kinetics studies in animals exposed by inhalation are extensive but all are single-exposure studies. No information is available in animals or humans following intermediate-duration exposure by the oral or dermal routes. A single kinetics study in rats exposed to plutonium by the oral route for an intermediate period indicated that significant deposition was found in the gastrointestinal tract, the skeleton, and soft tissues. Because limited or no data are available on systemic effects or kinetics following intermediate-duration exposure by all three routes, studies to provide such data would be useful. These data could be used to predict human health effects from exposure for this duration in populations living near hazardous waste sites and in the workplace, and to determine the relative contribution of each of the three routes of exposure to these adverse health effects.

Chronic Duration Exposure and Cancer. No information on noncancer health effects 'hollowing chronic exposure of animals or humans to plutonium by any route exists. Epidemiological studies generally report only mortality from cancer and do net report deaths from noncancer causes or other noncancer adverse effects that may have been identified. Limited kinetics studies of occupationally exposed individuals indicate that plutonium concentrations were higher in the lungs and trachealbronchial lymph nodes than in any other single organ, indicating that the lung would be the target organ for inhaled plutonium. However, no noncancer effects were reported in these individuals. Studies of kinetics following exposure by any route in laboratory animals are only for single exposures. Due to the general lack of data on noncancer health effects following chronic exposure, results of tests in animals exposed chronicaily to plutonium would be informative. Although, such tests may be difficult to design and carry out due to the radioactive nature of plutonium, it would be useful to compare such data to noncancer adverse effects which are commonly reported in single-dose studies. These studies would also be useful in evaluating toxicity, other than cancer, to the general public, as well as occupationally exposed individuals. In addition, it would be worthwhile to report information on noncancer effects seen in follow-up of existing occupational cohorts or new cohorts.

Studies in rats and dogs exposed to plutonium for 1 day have indicated that plutonium via inhalation causes cancer. At various times

following high doses of plutonium, tumors were found primarily in the lung, but aiso in the skeleton and liver. Chronic studies of animals exposed to plutonium via inhalation would be useful in order to compare the type of cancers that may occur and the onset of these effects to those reported in single-dose studies. Epidemiological studies have been equivocal. Most epidemiological studies of occupationally exposed individuals have consistently reported fewer cancer deaths in exposed cohorts than in an unexposed cohort or in the normal population. However, these epidemiological studies have many confounding factors including small cohort size, poorly defined exposure information, insufficient follow-up period, or possible concurrent exposure to external radiation. In one epidemiological study, the authors report a suggested increased risk of lymphopoietic cancers. However, the incidence of this type of cancer was based on limited data, and no increase in cancer incidence was noted in tissues with the highest concentration of plutonium as demonstrated in autopsy samples. Chronic animal studies at low radiation doses would be useful to provide information to assist in the interpretation of inconclusive carcinogenicity information from existing epidemiologic studies. No information is available on kinetics or development of cancer in animals or humans following oral or dermal exposure. Although acute studies report that absorption via these routes is much less than absorption via inhalation, chronic animal studies would provide information on kinetics and possible carcinogenicity of plutonium by these routes.

Genotoxicity. Epidemiological studies of occupationally exposed cohorts have reported equivocal results concerning exposure to plutonium and increased incidence of chromosomal aberrations. However, in vitro tests using human lymphocytes irradiated with plutonium demonstrated increases in sister chromatid exchange. Laboratory animals have exhibited increased chromosomal aberrations in blood lymphocytes following exposure to plutonium by inhalation. Other effects seen in vivo in animals include dominant lethality and reciprocal chromosomal translocation. In vitro tests using mammalian cells confirm the in vivo results. The evidence is clear that plutonium is genotoxic. However, more extensive study of individuals occupationally exposed would be useful, and would hopefully clarify the equivocal reports of previous studies.

Reproductive Toxicity. There are no data available regarding the reproductive toxicity of plutonium after inhalation, oral, or dermal exposure in either humans or animals. In laboratory animals given a single injection of a high dose of plutonium, significant fetal deaths were reported and were attributed to dominant lethality. Kinetics studies following single injection of plutonium indicate that plutonium is distributed to the testes or ovaries of laboratory animals (Green et al. 1976, 1977) and is retained there for an indefinite period of time (more than 575 days) (Green et al 1977; Taylor 1977). Although this

route of exposure is not relevant to humans, results of these studies would indicate that studies to evaluate reproductive effects in laboratory animals following single, repeated, or multi-generation exposure to piutonium via inhalation or ingestion would be worthwhile.

Developmental Toxicity. There are no data available regarding the developmental toxicity of plutonium after inhalation, oral, or dermal exposure in either humans or animals. However, results of kinetics studies in which animals were given a single injection of plutonium showed that plutonium crosses the placenta and is retained in the fetus (Green et al 1977; Sikov et al 1978b). These studies would indicate that additional data are needed to evaluate developmental effects in laboratory animals following single or repeated exposure to plutonium via inhalation or ingestion.

Immunotoxicity. There are no data available regarding immunotoxicity of plutonium after inhalation, oral, or dermal exposure in humans. In dogs exposed to plutonium via inhalation for a single day, damage to lymph nodes was observed in conjunction with pneumonitis (Gillett et al. 1988). Once plutonium particles have been deposited in the lung, macrophages play a role in the clearing process. In this clearing process, macrophages phagocytize plutonium particles and ultimately deposit them in the lymph nodes. This mechanism may lead to secondary damage to the lymph nodes and thus to the immune system. In dogs given a single subcutaneous injection of plutonium, damage to lymph nodes draining the injection site, as well as lymphopenia, were observed (Dagle et al. 1984.). The studies in dogs, together with knowledge of the clearing process in the lung, indicate that studies designed to evaluate the direct toxic effects of plutonium on the function of the immune system would be useful.

Neurotoxicity. No studies have been done to determine the neurotoxicity of plutonium. However, cells and tissues of the nervous system may be less radiosensitive than faster regenerating cells of the gastrointestinal tract or pulmonary epithelium. Consequently, neuronal impairment would not be expected. For this reason, tests of the neurotoxicity of plutonium may not be necessary at this time.

Epidemiological and Human Dosimetry Studies. Epidemiological studies of occupational cohorts with long-term exposure to plutonium include those established from employees at Los Alamos National Laboratory, the Rocky Flats Facility, and the Hanford Facility, as well as the cohort involved in the original Manhattan project at Los Alamos. These studies have failed to demonstrate an unequivocal association between exposure to plutonium and mortality from cancer following occupational exposure. However, these studies contain many limitations including small cohort size, poorly defined exposure information, or insufficient follow-up periods. Because these occupational cohorts have

been exposed to plutonium levels many times higher than environmentally exposed populations, continuation of the follow-up of these cohorts would generate useful information. Examination of these cohorts for end points-other than cancer, such as genetic effects and effects on the immune system, would be useful.

Epidemiological studies in which humans were occupationally exposed to plutonium attempted to correlate adverse health effects with body burdens of plutonium. However, definite correlations between plutonium exposure and body burdens have not been reported. Further information in this area is needed. Epidemiological studies in which activity concentrations in the workplace are reported also are needed. If an epidemiological study were conducted in which activity concentrations the workplace were known, attempts could be made to correlate exposure levels with body burdens, as well as with health effects. Isolated measurement of plutonium levels resulting from fallout have been made air, water, food, and soil. Overall, information regarding levels of plutonium in the environment is limited. If epidemiologic data could provide dose-response information, additional studies on environmental levels could provide information to evaluate the extent of the hazard associated with environmental plutonium exposure or exposure to individuals living near hazardous waste sites.

Biomarkers of Exposure and Effect. Currently, the only biomarker of exposure that has been identified is the presence of radioactivity released by plutonium, in the urine. The presence or this activity in the urine is specific to plutonium exposure and can be used to monitor short-term, intermediate, or long-term exposure. Although the detection of plutonium radioactivity in the urine is not a direct measurement of exposure, estimates may be derived using mathematical models. Other biomarkers of exposure may exist, such as the presence of plutonium in blood, bone, teeth, or hair.

Biomarkers of health effects resulting from plutonium-released radiation are not known. It is possible that early damage to bone marrow resulting from radiation exposure may be indicated by a decrease in stem cells or by a decrease in the number of red blood cells (Joshima et al. 1981). It is also possible that abnormal sputum cytology may be used as an early indicator of radiation damage to lung tissue (ATSDR 1990). Although a decrease in stem cells and abnormal sputum cytology may indicate exposure to radiation, additional research to determine if these methods are reliable and to correlate these effects with plutonium exposure levels would be worthwhile.

Absorption, Distribution, Metabolism, and Excretion. For laboratory animals, detailed quantitative information is available regarding the absorption, distribution, and excretion of plutonium compounds following acute exposure bv inhalation or injection. There is

no information on the toxicokinetics of plutonium following chronic exposure to low levels, and studies in this area would be more applicable to human exposure situations than single exposure studies. Information concerning the toxicokinetics of plutonium in adult animals following oral exposure is available. However, previous animal studies have indicated that very little plutonium is absorbed following oral exposure. Therefore, studies of kinetics following oral exposure are not needed at this time. Studies of age-related changes in the toxicokinetics of plutonium would be very valuable, especially those age-related differences that may indicate enhanced exposure or susceptibility. Very little is known regarding the absorption, distribution, and excretion of plutonium compounds following dermal exposure. However, it appears that the skin is an effective barrier against most plutonium compounds.

Comparative Toxicokinetics. There is limited information regarding comparative toxicokinetics among laboratory animal species and humans. However, similar target organs have been identified among laboratory animals exposed to plutonium. Toxic effects that have been observed in animals have not been observed in humans. In addition, hamsters develop many of the toxic effects in the lung following exposure to inhaled plutonium, but have not been found to develop lung tumors. This may be indicative of differences in anatomy and physiology or species sensitivity. Information to help identify the appropriate animal model to provide insight into the toxicokinetics of plutonium compounds in humans would be useful.

2.8.3 On-going Studies

G.L. Voelz (Los Alamos National Laboratory) is investigating the correlation between low-level plutonium and/or external radiation exposure and lung cancer incidence or other diseases among current and former workers at Rocky Flats, Los Alamos, Mound, Savannah River, Oak Ridge, and Hanford.

Mechanisms of alpha-emitting and bone-seeking radionuclide-induced skeletal cancers are being investigated by W.S. Jee (University of Utah) in humans and dogs.

The long-term toxicity of inhaled plutonium-239 dioxide (B.A. Muggenburg and his colleagues, Inhalation Toxicology Research Institute and F.W. Bruenger, University of Utah) in juvenile and mature beagle dogs is being studied. Influence of age at the time of exposure is the focus of the studies. Studies by Muggenburg include single and multiple exposure of rats, Syrian hamsters, and mice to plutonium-239 dioxide aerosols similar to human exposure.

2. HEALTH EFFECTS

J.H. Die1 (Inhalation Toxicology Research Institute) has been studying health effects in laboratory animals following repeated exposure to insoluble plutonium over a long fraction of their lifetime. Single exposures at comparable radiation dose levels are included for comparison. Experiments using rats and dogs are still in progress. whereas experiments using mice and hamsters have been completed.

The effects of inhaled plutonium-239 nitrate (G.E. Dagle, Pacific Northwest Laboratories), or plutonium-239 dioxide or plutonium-238 dioxide (J.F. Park, Pacific Northwest Laboratory), on lifespan have been under investigation in beagle dogs. The current investigation by Dagle involves determining the interrelationship of lung cancer, bone cancer, and noncancerous lesions in dogs exposed to low levels of plutonium. Park is continuing to investigate the mechanisms of lymph node damage and lymphopenia in these animals. The role of oncogenes in plutoniuminduced cancers will be examined in both studies by Dagle and Park. Furthermore, M.E. Frazier (Pacific Northwest Laboratory) is studying whether oncogenes are activated in plutonium-induced lung cancer or whether oncogene activation is a cause or an effect of cancer development.

An extensive investigation of the effects of lifetime inhalation of low-levels of plutonium-239 dioxide ($5x10^{+2}$ to $1.9x10^{-5}$ pCi ($1.9x10^{1}$ to $7.0x10^{3}$ Bq) initial alveolar depositions] in rats is in progress by C.L. Sanders (Pacific Northwest Laboratory).

Among the few studies in progress pertaining to plutonium genotoxicity is the investigation of heritable plutonium-induced gene mutations, chromosome aberrations, and dominant lethal mutations in mice (P.B. Selby, Oak Ridge National Laboratory). P.G. Kale at Hampton University is studying the genetic effects of plutonium in Drosophila. Special emphasis will be placed on the dose-response relationship in predicting consequences of low-level plutonium exposures.

Current studies by S.E. Dietert at Hanford Environmental Health Foundation focus on elucidating the biokinetics and dosimetry of plutonium and related elements in humans. The study includes determining the distribution and concentration of transuranic elements in man by radiochemical analysis of donated autopsy tissues from occupationally exposed individuals. The uptake and distribution patterns of plutonium and other actinides in humans are being studied by J.F. McInory (Los Alamos National Laboratory). N.P. Singh at the University of Utah is studying the biological half-lives of plutonium in liver and bone of the general population of northern Utah.

M.F. Sullivan at Pacific Northwest Laboratory is investigating the transfer factors involved in the absorption of plutonium in animals and other actinides across the gastrointestinal tract under conditions that may be experienced by humans (such as the oxidation state of plutonium,

fasting, high acidity, iron and calcium deficiency). Plutonium gastrointestinal tract absorption is being studied in three baboons in order to obtain information on possible human gastrointestinal tract absorption of plutonium (M.H. Battacharyya, Argonne National Laboratory).

R.G. Cuddihy at Inhalation Toxicology Research Institute is studying the mechanisms involved in the deposition and clearance of inhaled plutonium in the respiratory tract of rats and other animals.

E. Shek (Pharmatec) is investigating methods for improving gastrointestinal tract absorption of orally administered chelating agents, which bind metals such as plutonium and facilitate excretion from the body. New actinide-chelating agents produced by microorganisms are being tested by P.W. Durbin at Lawrence Berkeley Laboratory. It is assumed that these agents bind plutonium(IV) and enhance its excretion. Another study by Durbin includes the development of metabolic models for plutonium and other radionuclides in order to verify and/or modify metabolic models currently recommended by the International Commission on Radiation Protection (ICRP) for these radioelements.

S.C. Miller (University of Utah) is determining the localization and distribution of plutonium-239 and other actinides in tissue, cellular, and subcellular compartments of the gonads (testes and ovaries) in different species and in human tissue.

R.E. Filipy (Pacific Northwest Laboratory) is continuing the investigation of the effects of cigarette smoke on rats and dogs exposed to plutonium as compared to sham-exposed animals or those exposed to plutonium alone. The findings of the study will contribute to the understanding of the potential health effects of inhaled plutonium among the cigarette-smoking population.

3. CHEMICAL AND PHYSICAL INFORMATION

3.1 CHEMICAL IDENTITY

The chemical formula and identification numbers for plutonium are listed in Table 3-1.

3.2 PHYSICAL AND CHEMICAL PROPERTIES

Important physical and chemical properties of plutonium and its compounds are listed in Table 3-2. There are 15 known isotopes of plutonium which have atomic weights ranging from 232 to 246. Of these. only plutonium isotopes 236 to 243 are of particular biological interest either as a result of their production in nuclear processes or because of other uses (Nenot and Stather 1979). Therefore, only these isotopes are listed in the tables. The radiological properties for plutonium isotopes are presented in Table 3-3. Decay schemes for plutonium-239 and plutonium-241 are given in Figure 3-l and Figure 3-2.

Plutonium is a very reactive metal and oxidizes readily in moist air. In finely divided form, plutonium metal is pyrophoric (Taylor 1973). Plutonium exhibits five oxidation states from plutonium(II1) to plutonium(VI1). The four lower oxidation states are stable in solution and may co-exist in the same solution. Complex (coordination) compounds are formed with many of the common inorganic anions, such as plutonium nitrate ($Pu(NO_3)_4$).

A large number of plutonium compounds have been prepared in the solid state. Plutonium metal is attacked by all common gases at elevated temperatures; thus ammonia and nitrogen form nitrides, hydrogen forms hydrides, the halogens and gaseous halogen acids produce halides, carbon monoxide forms carbides, and carbon dioxide produces carbides and dioxides (Cleveland 1970). An in-depth review of the chemistry of plutonium and its compounds is given in Cleveland (1970).

TABLE 3-1. Chemical Identity of Plutonium and Selected Plutonium Compounds[a]

Property	Value					
	Plutonium	Plutonium Dioxide	Plutonium Nitride	Plutonium Hexafluoride	Plutonium Oxalate	Plutonium Tetrafluoride
Chemical name	Plutonium	Plutonium dioxide	Plutonium nitride	Plutonium hexafluoride	Plutonium oxalate	Plutonium tetrafluoride
Isotopes	Plutonium-236 Plutonium-237 Plutonium-238 Plutonium-239 Plutonium-240 Plutonium-241 Plutonium-242 Plutonium-243	No data	No data	No data	No data	No data
Trade names[b]	Plutonium metal	Oxide	Nitride	Halide	Oxalate complex	Halide
Chemical formula	Pu	PuO_2	PuN	PuF_6	$Pu(C_2O_4)_2 \cdot 6H_2O$	PuF_4
Chemical structure	No data	No data	No data	No data	No data	No data
Identification numbers:						
CAS Registry[c]	7440-07-5	No data	No data	No data	No data	No data
NIOSH RTECS	No data	No data	No data	No data	No data	No data
EPA Hazardous Waste	No data	No data	No data	No data	No data	No data
OHM/TADS	No data	No data	No data	No data	No data	No data
DOT/UN/NA/IMCO[d] Shipping	UN 2918	No data	No data	No data	No data	No data
HSDB	No data	No data	No data	No data	No data	No data
NCI	No data	No data	No data	No data	No data	No data

CAS = Chemical Abstract Service
DOT/UN/NA/IMCO = Department of Transportation/United Nations/North America/International Maritime Dangerous Goods Code
EPA = Environmental Protection Agency
HSDB = Hazardous Substance Data Base
NCI = National Cancer Institute
NIOSH = National Institute for Occupational Safety and Health
OHM/TADS = Oil and Hazardous Materials/Technical Assistance Data System
RTECS = Registry of Toxic Effects of Chemical Substances

[a]Source: Weast 1980, unless otherwise stated.
[b]Trade names were obtained from Taylor 1973.
[c]CAS Registry number obtained from Windholz 1983.
[d]DOT identification number obtained from 49 CFR 172.101 1988.

TABLE 3-2. Physical and Chemical Properties of Plutonium and Selected Plutonium Compounds[a]

Property	Value					
	Plutonium	Plutonium Dioxide	Plutonium Nitride	Plutonium Hexafluoride	Plutonium Oxalate	Plutonium Tetrafluoride
Molecular weight	242.00	274.00	256.01	355.99	526.13	317.99
Color	Silver-white	Yellowish-green	Black	Reddish-brown	Yellowish-green	Pale brown
Physical state[b]	Metal	Solid	Hard solid	Solid	Solid	Solid
Melting point, °C	639.5	2200-2400	No data	50.75	No data	No data
Boiling point, °C	3232	No data	No data	62.3	No data	No data
Density at 20°C	19.84	11.46	14.25	No data	No data	7.0
Odor	Odorless	No data	No data	No data	No data	No data
Odor threshold:						
Water	No data	No data	No data	No data	No data	No data
Air	No data	No data	No data	No data	No data	No data
Solubility:[b]						
Water at 20°C	No data	No data	Hydrolized in cold water	Decomposes in cold water	Insoluble in water	Insoluble in water
Organic solvents	No data	No data	No data	No data	No data	No data
Partition coefficients:						
Log octanol/water	No data	No data	No data	No data	No data	No data
Log Koc	No data	No data	No data	No data	No data	No data
Vapor pressure	No data	No data	No data	No data	No data	No data
Henry's law constant	No data	No data	No data	No data	No data	No data
Autoignition temperature	No data	No data	No data	No data	No data	No data
Flashpoint	No data	No data	No data	No data	No data	No data
Flammability limits	No data	No data	No data	No data	No data	No data
Valence state	+3,+4,+5,+6,+7	No data	No data	No data	No data	No data

[a]Source: Weast 1980, unless otherwise noted.
[b]The physical state for all compounds and the solubility for PuF_4 were obtained from Taylor (1973).

TABLE 3-3 Radiological Properties of Plutonium Isotopes[a]

Isotope	Half-life (years)	Decay Modes and Energy[b] (Mev)	Decay Product[c]	Specific Activity (μCi)/gm)
^{236}Pu	2.85	α, 5.75 SF, 5.722	Uranium-232	5.32×10^{8}
^{237}Pu	0.125	EC, 0.22	Uranium-233	1.21×10^{10}
^{238}Pu	87.8	α, 5.46 SF, 5.456	Uranium-234	1.71×10^{7}
^{239}Pu	24,390.0	α, 5.243	Uranium-235	6.13×10^{4}
^{240}Pu	6,537.0	α, 5.255 SF, 5.123	Uranium-236	2.28×10^{5}
^{241}Pu	15.02	ß, 0.0208	Americium-241	9.90×10^{7}
^{242}Pu	387,000.0	α, 4.89	Uranium-238	3.82×10^{3}
^{243}Pu	56,600.0	ß, 0.59	Americium-243	2.60×10^{12}

SF = Spontaneous Fission
EC = Electron Capture

[a]Source: Nenot and Stather (1979), unless otherwise stated.
[b]Spontaneous fission and electron capture energies obtained from Weast (1980).
[c]Decay product information derived from Walker et al. (1977).

Am							
Pu	239 Pu 24,065 yrs						
Np	↓						
U	235 U 7.038E8 yrs						
Pa	↓	231 Pa 3.276E4 yrs					
Th	231 Th 25.52 hrs	↓	227 Th 18.718 days				
Ac		227 Ac 21.773 yrs	↓				
Ra			223 Ra 11.43 days				
Fr			↓				
Rn			219 Rn 3.96 s				
At			↓				
Po			215 Po 0.001780 s				
Bi			↓	211 Bi 2.14 min			
Pb			211 Pb 36.1 min	↓	207 Pb stable		
Tl				207 Tl 4.77 min			

↓ alpha decay

↗ beta decay

Figure 3-1. Plutonium-239 Decay Series

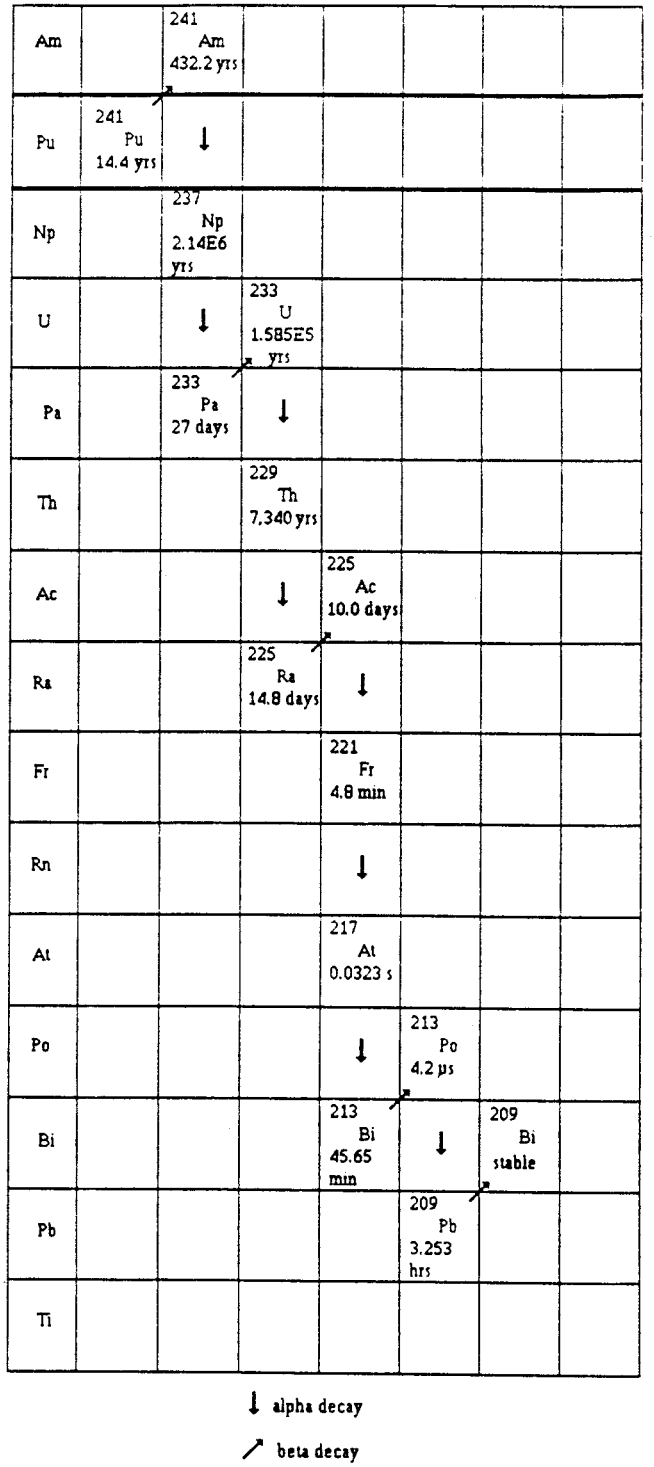

Figure 3-2. Plutonium-241 Decay Series

4. PRODUCTION, IMPORT, USE, AND DISPOSAL

4.1 PRODUCTION

Plutonium exists in trace quantities in naturally occurring uranium ores (Weast 1980). Plutonium is produced by the bombardment of uranium with neutrons. The most important isotope, plutonium-239, is produced in large quantities from natural uranium in nuclear reactors (Weast 1980). Plutonium-240, -241, and -242 are produced from successive absorption of neutrons by the plutonium-239 atoms. The successive absorption of two neutrons rather than one by uranium leads to the production of plutonium-238. Plutonium-237 is usually produced by the helium ion bombardment of uranium-235.

During neutron bombardment of plutonium-239 and -241, fission occurs in addition to neutron capture. With plutonium-239 about 70% undergoes fission, while the remainder is transmuted to plutonium-240. With plutonium-241, 20% undergoes fission and the remainder is transmuted to plutonium-242 (Choppin and Rydberg 1980).

The plutonium in spent uranium fuel from light water reactors (LWR) is 56% plutonium-239, 26% plutonium-240, 12% plutonium-241, 5% plutonium-242, and 1% plutonium-238 (Choppin and Rydberg 1980). This composition will vary with other types of reactor fuel, but this type is the most common in reactors operating in the United States.

As of 1980, the world's nuclear power reactors were producing more than 20,000 kg of plutonium per year (Weast 1980). In addition to these, the United States Department of Energy (DOE) has operated nuclear reactors to produce nuclear materials for the nation's defense program. These include plants at Savannah River, South Carolina, and the Hanford Works in Richland, Washington.

4.2 IMPORT

There is no information on the importation of plutonium. However, small quantities of nonweapon plutonium have been produced at the Atomic Energy Commission's (now Department of Energy) production reactors for foreign sales (Liverman et al. 1974).

4.3 USE

The majority of the plutonium, in the form of plutonium-239, is used as an ingredient in nuclear weapons. As a result of the atmospheric testing of these weapons during the 1950s, plutonium has been dispersed throughout the atmosphere. An estimated 400 kCi (1.5×10^{16} Bq) plutonium-239 and -240 were produced during weapons testing, of which approximately 325 kCi (1.2×10^{16} Bq) was globally dispersed (Bennett 1976a). Four hundred kCi of plutonium-239 weighs approximately 4,600 kg. Approximately 100,000 kCi (3.7×10^{12} Bq)

plutonium have been dispersed within our environment from about 400 nuclear explosive tests, including those by the United States, Great Britain, and the Soviet Union between 1945 and 1963 (Facer 1980).

The nuclear reactors at the Richland and Savannah River plants were built to produce nuclear materials for the nation's defense program. The amounts of plutonium involved in the weapons program are necessarily classified.

Plutonium-238 is used as a heat source in thermo-electric power devices, such as have been employed on various satellites and had been proposed for powering artificial hearts (Bair and Thompson 1974). The estimated total quantity of plutonium-238 required for these applications through the year 2000 ranges from 25 to 75 kg (430 to 1,300 kCi; 1.6×10^{16} to 4.8×10^{16} Bq) (Liverman et al. 1974).

4.4 DISPOSAL

Plutonium is considered a transuranium (having an atomic number greater than that of uranium) element. It has a very long radiolcgical half-life (86 and 24,000 years for plutonium-238 and -239, respectively), and, therefore, the radioactivity diminishes very slowly. Spent nuclear fuel is not reprocessed in the United States at the present time, and the fuel must be disposed of intact (Lamarsh 1983). The usual method of disposal has been to place the fuel in suitable containers and bury them in a waste repository. Prior to 1970 solid wastes containing radioactive wastes generated by nuclear power plants were buried at commercial waste sites located at Sheffield, Illinois; Beatty, Nevada; Morehead, Kentucky; Richland, Washington; and West Valley, New York. As of 1974, approximately 80 kg of plutonium was contained in this waste (Daly and Kluk 1975).

At present, radioactive wastes are being held at the DOE facilities including those in Richland, Washington, Savannah River, South Carolina, and at other reactor sites. These transuranic wastes are stored either above ground or in shallow burial pits. Neither of these methods are intended as long-term storage solutions.

5. POTENTIAL FOR HUMAN EXPOSURE

5.1 OVERVIEW

Plutonium is a radioactive element produced by neutron capture and beta decay of uranium-238 (or other elements), both naturally (in minuscule amounts) and as a result of human activities. Plutonium is found in the environment in the form of several isotopes. The source of plutonium can be traced based on the isotope or isotopes detected in a sample. Plutonium is found naturally in uranium-rich ores in concentrations of one part per 1Orr parts uranium (i.e., $1x10^{-11}$ kg plutonium/kg uranium) (Leonard 1980).

The principal plutonium isotopes used in commerce and by the military are plutonium-238 and plutonium-239. These two isotopes are used because of their ease of production and their relatively long halflives. Plutonium-238 is used in thermoelectric generation systems in spacecraft, cardiac pacemakers, and other power sources (Harley 1980; NEA/OECD 1981). Plutonium-239 and -240 are produced in nuclear power plants as a product of nuclear fission as well as in production facilities for use in nuclear weapons.

Possible sources of plutonium to the environment include: weapons testing, accidents involving weapons transport, nuclear reactors and radioisotope generators, fuel processing and reprocessing, and fuel transport (NEA/OECD 1981). Plutonium-239 is generated in irradiated uranium fuel when neutrons are captured by uranium-238 nuclei. Some of the plutonium-239 is consumed during the operation of the reactor. Production of plutonium by nuclear reactors generating electricity and by weapons production was estimated at $3.8x10^{6}$ kg in 1978 (NEA/OECD 1981).

Atmospheric testing of nuclear weapons has been the main source of plutonium dispersed in the environment. Accidents and routine releases from weapons production facilities are the primary sources of localized contamination. Consumer and medical devices containing plutonium are sealed and are not likely to be environmental sources of plutonium (WHO 1983). Plutonium released to the atmosphere reaches the earth's surface through wet and dry deposition to the soil and surface water. Once in these media, plutonium can sorb to soil and sediment particles or bioaccumulate in terrestrial and aquatic food chains.

According to the NPL database (VIEW 1989), plutonium has been identified above background levels at five NPL sites. Plutonium-238 has been identified at three of these sites, plutonium-239 at five sites, and plutonium-240 at one site. The frequency of these sites within the United States can be seen in Figure 5-l.

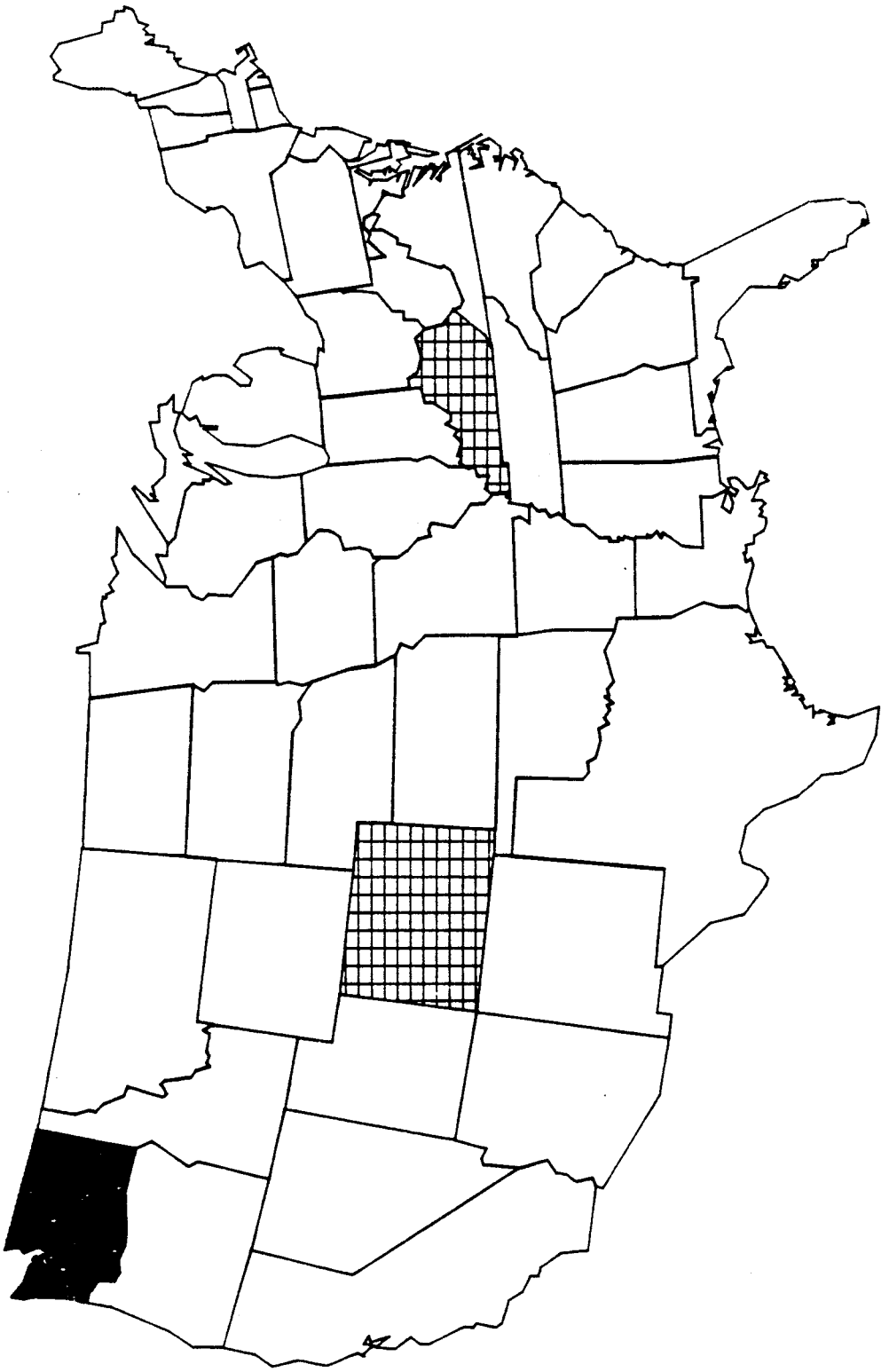

FIGURE 5-1. FREQUENCY OF SITES WITH PLUTONIUM CONTAMINATION

5.2 RELEASES TO THE ENVIRONMENT

5.2.1 Air

Anthropogenic (man-made) releases of plutonium are the primary sources of plutonium to the atmosphere. Atmospheric testing, fires involving plutonium-containing materials, and routine releases due to normal activities at processing and generating plants are a11 potential sources of airborne plutonium. Resuspension of plutonium sorbed to contaminated surface soils via fugitive dust emissions is an indirect pathway by which plutonium may be re-released into the atmosphere (Harley 1980).

Plutonium released during nuclear weapons testing is the largest source of plutonium-239 and -240 in the environment (Harley 1980). Approximately 320 kCi ($1.2x10^{16}$ Bq) of plutonium-239, -240 and 9 kCi ($3.3x10^{14}$ Bq) of plutonium-238 have been released to the atmosphere by nuclear tests and distributed worldwide (Eisenbud 1987). Concentrations of transuranics introduced into the environment through underground test venting, accidents involving United States nuclear weapons, and releases during weapon production operations have been negligible in comparison with those released during atmospheric testing of nuclear explosives in the 1960s (Facer 1980).

In April, 1964, a Transit Navigational Satellite was launched in California with a payload that included a Satellite for a Nuclear Auxiliary Power Generator (SNAP-9A) containing 17 kCi ($6.3x10^{14}$ Bq) of plutonium-238. The rocket system failed and the satellite reentered the atmosphere in the Southern Hemisphere and burned over the Indian Ocean at an altitude of about 50 km (Harley 1980). The destruction of the SNAP-9A resulted in the largest single release of plutonium-238 to the atmosphere, primarily in the form of very small oxide particles (Harley 1980).

Research facilities and plants have also released plutonium to the atmosphere. For example, the Mound Plant in Miamisburg, Ohio, released about 0.03 kCi ($1x10^{10}$ Bq) to the atmosphere from.the beginning of its operation through 1976 (NEA/OECD 1981). A commercially operated reprocessing plant in West Valley, New York, has reportedly released 0.000005 kCi ($1.7x10^{8}$ Bq) to the atmosphere over the course of 6 years (NEA/OECD 1981).

5.2.2 Water

Fallout from atmospheric weapons testing, accidents involving nuclear weapons, planned as well as accidental reactor effluent releases, and disposal of radioactive wastes are all means by which plutonium can be introduced into water systems (Harley 1980; NEA/OECD 1981). In a typical 1,000 megawatt electric (MWe) light water reactor

in a nuclear power plant about 200 kg of plutonium [equivalent to 13 kCi (4.8×10^{14} Bq); one curie of plutonium-239 - 16g] are generated per year of operation in the spent fuel (NEA/OECD 1981; Facer 1980). Contaminated cooling water containing plutonium from nuclear production facilities may have been discharged into oceans or rivers. If release occurs from waste containers, buried radioactive wastes may migrate or seep into groundwater (NEA/OECD 1981). As an example of plant emissions, the Mound Plant in Miamisburg, Ohio, discharged a total of about 0.0005 kCi (1.9×10^{10} Bq) plutonium-238 into a river near the site from the beginning of its operation through 1976 (NEA/OECD 1981).

In January, 1968, while attempting to make an emergency landing, a United States military aircraft with four nuclear weapons on board crashed in Thule, Greenland. The impact resulted in detonation of the high explosives in all four nuclear weapons aboard. The oxidized plutonium was dispersed by both the explosion and the fire involving the fuel in the jet (Harley 1980). Amounts of plutonium released to the air in this accident have been estimated at 0.024 kCi (9×10^{11} Bq) of insoluble plutonium (NEA/OECD 1981). .The maximum concentration of plutonium in ocean sediments was found 1 km from the point of impact. The sediment-bound plutonium was found to migrate both downward in the sediment column and horizontally from the point of impact. The concentrations decreased with distance from the point of impact.

Sediments can act as both a repository for and a source of waterborne plutonium. Atmospheric fallout reaching surface water can settle in the sediments. The plutonium in the ocean sediments at Bikini Atoll, for example, was found to be resuspended and released to the bottom waters (Schell et al. 1980). In a freshwater waste pond at the Hanford reactor, plutonium was found to be bound to the sediments and was not available for uptake by plants or animals in the pond (Emery et al. 1980). The difference between the observations in the two ecosystems may be due to the dynamic nature of the ocean water near Bikini Atoll versus the relatively static nature of a waste water pond.

5.2.3 Soil

Plutonium has been detected in extremely small amounts as a naturally occurring constituent of some minerals and ores. Uranium and thorium ores in Canadian pitchblende, Belgium Congo pitchblende, Colorado pitchblende, Brazilian monazite, and North Carolina monazite have been found to contain plutonium-244 at a weight ratio of up to 9.1×10^{-12} kg plutonium/kg ore (Leonard 1980).

Soils may become contaminated from fallout associated with nuclear weapons tests, such as those conducted at the Trinity Site in southern New Mexico, the Pacific Proving Ground at the Enewetak Atoll, and the Nevada Test Site or with accidental, non-nuclear detonation of nuclear weapons, such as occurred at Palomares, Spain. Research facilities,

such as the Los Alamos National Laboratory, Los Alamos, New Mexico, may release treated radioactive wastes under controlled conditions. Production facilities, such as the Hanford and Savannah River Plants and experimental reactor stations, for example, the Idaho National Engineering Laboratory, Idaho Falls, Idaho, also released treated plutonium-bearing radioactive wastes under controlled conditions to soils (Hanson 1975).

Atmospheric weapons testing fallout has been a global source of transuranics, including plutonium, in soils (Harley 1980; NEA/OECD 1981). It has been estimated that approximately 100 kCi (3.7×10^{15} Bq) of plutonium from weapons have been distributed globally from all testing sources and could be environmentally available. Of that amount, approximately 1.0 to 10 kCi (3.7×10^{11} to 3.7×10^{12} Bq) were deposited on test site surface soils in the United States (Facer 1980).

Several of the major nuclear facilities in the United States use plutonium and some of these have released plutonium to the environment. These releases have taken place at remote sites and generally have not been measurable outside the plant property. Approximately 0.002 kCi (7.4×10^{10} Bq) of plutonium have been disposed in the Los Alamos National Laboratory canyon waste disposal sites (Harley 1980). The Savannah River Plant, Aiken, South Carolina, has released a total of 0.005 kCi (1.6×10^{11} Bq) of plutonium to local soil (Harley 1980). Leakage of stored waste released between 0.01 and 0.1 kCi (3.7×10^{11} and 3.7×10^{12} Bq) of plutonium to the soil over a period of several years at the Rocky Flats facility, Golden, Colorado (Facer 1980). A break in a waste transfer line caused the release of about 0.3 kCi (1.1×10^{13} Bq) of plutonium-238 at the Mound Plant, Miamisburg, Ohio, in 1969 (Facer 1980).

A fire on May 11, 1969, occurred at the plutonium processing facility at Rocky Flats, Golden, Colorado. Subsequently, a study of the plutonium content in off-site soils was performed. The results of the study indicated that the plutonium found off-site was due, primarily, to small emissions from the facility rather than to the fire, and that a total of 0.003 kCi (9.6×10^{10} Bq) of plutonium was deposited in soils within a 7 mile radius from the facility (Eisenbud 1987).

Another source of soil contamination at Rocky Flats was the leakage of plutonium-contaminated oil. Plutonium was present as the dioxide when it was released. The dioxide was then adsorbed to the soil. Fugitive dust emissions caused plutonium-contaminated soil to be distributed away from the spill. Most of the plutonium remained on the surface, although some was released and migrated downward through the soil column (Little and Whicker 1978).

A United States military aircraft carrying four nuclear bombs collided with a tanker aircraft during refueling in Palomares, Spain, in

January, 1966. The bombs broke free of the airplane and the high explosive in two of the weapons detonated when the bombs hit the ground. Initial surveys showed that 0.00003 Ci piutonium/m^2 ($1.2x10^6$ Bq/m^2), in the form of a finely powdered dioxide, were spread over 2 hectares (20,000 m^2) (Harley 1980).

5.3 ENVIRONMENTAL FATE

5.3.1 Transport and Partitioning

Plutonium enters the environment primarily through releases to the atmosphere or direct discharge to ponds, streams, or oceans. Emissions to the atmosphere will result in plutonium fallout. In the case of weapons testing, approximately one-fifth of the plutonium released falls on the test site (Harley 1980). The rest is carried in the atmosphere, adsorbed to particulate matter and is transported back to earth via dry or wet deposition. Once plutonium is deposited either on the land or surface water, sorption to soils or sediments is the primary environmental fate of plutonium. A small fraction of plutonium reaching the soil will become solubilized either through chemical or biological processes, depending upon its chemical form. In soluble form, plutonium can either migrate in groundwater or surface water or be available for uptake into plants.

Atmospheric releases of plutonium occur as a result of nuclear weapons testing or routine or nonroutine nuclear reactor operations and fuel reprocessing. The rate at which plutonium is removed from the atmosphere will depend on the chemical and physical properties of particles to which it is adsorbed, as well as the meteorological conditions. The larger the particles, the faster fallout will occur. The particle size expected to be released from either of the above mentioned sources ranges from 0.3 pm to 1.1 pm. Based on computer modeling, these particles are expected to reach the earth's surface within 60 days of their release (NEA/OECD 1981). The global fallout rate of plutonium-238, predominantly from the SNAP-9 accident, as determined by Harley (1980), is 0.002 pCi/m^2/day ($7.4x10^{-5}$ Bq/m^2/day) based on plutonium levels measured in surface soils. The global deposition rate of plutonium-239 and plutonium-240 combined is equal to 0.03 pCi/m^2/day ($1.1x10^{-3}$ Bq/m^2/day) (Corey et al. 1982).

Plutonium deposited on soil surfaces may be resuspended in the atmosphere especially in areas that have low soil moisture levels, such as the Nevada Test Site. In drier areas, the levels of ambient airborne dust are expected to be higher than in areas with normal rainfall (Harley 1980). The highest concentrations of plutonium are likely to be found in the fine silt-clay particle size range. Particles of this size tend to be transported the farthest distance by wind and water (WHO 1983).

5. POTENTIAL FOR HUMAN EXPOSURE

The transport and partitioning of plutonium in soils depends on the form of the compound. The solubility of plutonium depends on the properties of the soil, the presence of organic and inorganic complexing, agents, the form of plutonium that enters the soil environment, and the presence of soil microorganisms (Bell and Bates 1988; Kabata-Pendias and Pendias 1984; WHO 1983; Wildung and Garland 1980). Plutonium fallout from the atmosphere, for example, tends to be deposited primarily as the insoluble dioxide (Harley 1980; Wildung et al. 1987). The majority of plutonium remains within the top few centimeters of the soil surface as the dioxide form (WHO 1983). Microorganisms can change the oxidation state of plutonium, thereby either increasing or decreasing its solubility.

Plutonium will migrate in soils as the hydrolyzed ion or as a complex, formed with organic or inorganic acids. Mewhinney et al. (1987b) found that particles subjected to wetting and drying, such as those found on the soil surface, released more plutonium than soils continually immersed in a solvent, such as that found in lakes. This phenomenon is attributed to the formation of a soluble dioxide layer on the particle's surface during the drying phase. Soil organisms have also been found to enhance the solubility of plutonium (Wildung et al. 1987). Once plutonium enters the soluble phase, it then becomes available for uptake by plants. The plutonium(IV) oxidation state is found in plants due to its ability to hydrolyze in the environment (Garland et al. 1981, 1987). Cataldo et al. (1987) postulate that reduction of the higher oxidation states, such as plutonium(VI), occurs prior to absorption/transport across the root membrane.

The behavior of plutonium in surface waters is dependent upon the oxidation state and the nature of the suspended solids and sediments. Plutonium(II1) and plutonium(IV) are considered to be the reduced forms of plutonium while plutonium(V) and plutonium(V1) are the oxidized forms. The oxidized forms of plutonium are found in natural waters when the concentrations of dissolved organic matter or dissolved solids are low (Nelson et al. 1987). Humic materials (naturally occurring organic acids) were found to reduce plutonium(V) to plutonium(IV) in sea water. This was followed by adsorption of plutonium(IV) onto iron dioxides and deposition into the sediments (Choppin and Morse 1987).

The partitioning of plutonium from surface water to sediments in freshwater and marine environments depends on the equilibrium between plutonium(IV) and plutonium(V), and the interaction between plutonium(IV) in solution and plutonium sorbed onto sediment particle surfaces (NCRP 1984). Sorption onto marine clays was found to be largely irreversible (Higgo and Rees 1986). Higgo and Rees (1986) also found that the initial sorption of plutonium onto clays was effective in removing most of the plutonium species that would be able to sorb onto the clay. When sorption to carbonate marine sediments was investigated, it was found that some desorption from the surface would also occur.

This behavior was due to the presence of plutonium carbonate complexes on the sediment surfaces which were sorbed less strongly than plutonium dioxide complexes (Higgo and Rees 1986). In fact, the formation of plutonium complexes with organic carbon causes plutonium to remain in solution as a complex (NCRP 1984).

Plutonium can be taken up from various environmental media into plants and animals. The highest concentrations of plutonium in plants are found in the roots where plutonium is present as a surface-absorbed plutonium complex, a stabilized complex, or as a soluble plutonium complex (Garland et al. 1981). The concentration of plutonium in soil can be compared with the concentration in plants to determine what fraction present in soil reaches the plant. Soil to plant concentration ratios of $1x10^{-6}$ to $2.5x10^{-4}$ plutonium in wet vegetation/plutonium in dry soil have been calculated based on radioisotope experiments in plants grown in controlled environments. The stems and leaves have lower overall concentrations of plutonium than the roots, but higher concentrations of soluble plutonium. The seeds were found to have low concentrations of plutonium, which indicated that plutonium was not very mobile in plants (Cataldo et al. 1987). In studies on orange trees, Pinder et al. (1987) found that plutonium-238 was deposited on the leaf or soil surface, remained there, and that no measurable quantities were transferred to the fruits. Grain crops grown near the Savannah River Plant, Aiken, South Carolina, were found to contain higher concentrations of plutonium the closer to the facility they were grown. During harvesting, plutonium from soils or straw was resuspended and mixed with the crop. Plutonium in vegetable crops grown at Oak Ridge National Laboratory, Oak Ridge, Tennessee, contained higher plutonium concentrations in the foliage biomass than in the fruit. Peeling of potatoes and beets removed 99% of the residual plutonium (Adriano et al. 1980).

Plutonium transferred from soil or plants to grazing herbivores was predominantly associated with the animal's pelt and gastrointestinal tract (Hakonson and Nyhan 1980). Rodents studied near the Los Alamos and Trinity sites in New Mexico support this claim. Hakonson and Nyhan (1980) found no evidence of bioconcentration through the food chain from soil to plants to rodents. They concluded that soil was the source of plutonium in rodents. In contrast, a study by Sullivan et al. showed that rodents absorbed more plutonium-238 when it was incorporated into alfalfa (by growing it in soil containing plutonium) than when it was administered in the inorganic form (Sullivan et al. 1980). This study suggests that plutonium bound to organic compounds may have increased availability. However, the authors indicate that further study is needed.

Plutonium was found to bioaccumulate in aquatic organisms, primarily at the lower end of the food chain. The bioconcentration factors (i.e., the amount of the chemical found in the organism divided

by the concentration in the surrounding water over the same time period) were 1,000 for mollusks and algae, 100 for crustacea, and 10 for fish (WHO 1983). Plutonium is concentrated in the bones of fish rather than in muscle tissues, as seen by whole fish to muscle tissue ratios of $2x10^6$ to $5x10^4$ or 40:1 (NCRP 1984).

5.3.2 Transformation and Degradation

Plutonium is formed and transmuted through radioactive decay. Three common types of radioactive processes involve the release of alpha or beta particles or gamma rays. Alpha decay results in the release of an alpha particle, which is a charged particle emitted from the nucleus of an atom having a mass and charge equal in magnitude to a helium nucleus (i.e., two protons and two neutrons). In alpha decay, the atomic mass of the nuclide is reduced by four and the atomic number by two. For example, plutonium-239 undergoes alpha decay.to form uranium-235.

Beta particles are charged particles emitted from the nucleus of an atom with a mass and charge equal in magnitude to that of an electron. In beta decay reactions, as the electron is ejected, the number of protons in the resulting atom increases, changing the atomic number of the atom but not the mass. For example, plutonium-241 undergoes beta decay to form americium-241.

A gamma ray is short wavelength electromagnetic radiation emitted from the nucleus. Nuclei which have undergone transmutation by alpha or beta decay or by capture of a neutron often return to the ground state by emission of gamma radiation. Addition of a neutron changes the atomic mass or isotope number of the element but not the atomic number, as seen by the formation of plutonium-242 from plutonium-241.

The chemical transformation reactions plutonium undergoes in the environment are primarily oxidation and reduction reactions. There are five oxidation states found in the environment. These are plutonium(III), plutonium(IV), plutonium(V), plutonium(VI), and plutonium(VI1). The last, plutonium(VII), is not commonly found and it is only found under very alkaline conditions. The dominant oxidation state of plutonium in the environment is plutonium(IV) (Wildung et al. 1987).

5.3.2.1 Air

Plutonium does not undergo transformation processes in the air beyond those related to radioactive decay. Radioactive decay will be important for the short-lived isotopes with half-lives less than the average residence time in the troposphere of approximately 60 days. For example, plutonium-237 has a half-life of 46 days and undergoes electron capture to form neptunium-237 which has a half-life of $2.1x10^6$ years

(Nero 1979). Therefore, neptunium-237 may form in the stratosphere prior to deposition of plutonium-237 on the earth's surface as fallout.

5.3.2.2 Water

The important chemical transformation process in surface water is the oxidation or reduction of plutonium. In waters with low suspended solids, plutonium is generally found in oxidized forms, dissolved in the water. In waters with high suspended solids, plutonium is generally reduced and sorbed onto either suspended solids or sediments (Choppin and Morse 1987; Higgo and Rees 1986; Nelson et al. 1987).

Plutonium behaves differently than many other inorganic elements il that it can exist simultaneously in four oxidation states over a range of pH values. Under acidic conditions, the nature of the complexing ligands present in solution will influence the oxidation state of plutonium. The presence of fulvic acid (a naturally occurring organic acid) facilitates the reduction of plutonium(IV) to plutonium(III), especially below pH 3.1. The reduction of the higher oxidation states appears to be even less dependent on pH, especially below pH 6 (Bondietti et al. 1976).

5.3.2.3 Soil

Plutonium found in soils may undergo the same oxidation/reduction reactions described for surface waters in places where soil contacts water. In addition to oxidation/reduction reactions, plutonium can react with other ions in soil to form complexes. These complexes may then be absorbed by roots and move within plants; however, the relative uptake by plants is low. In plants, the complex can be degraded but the elemental plutonium will remain.

5.4 LEVELS MONITORED OR ESTIMATED IN THE ENVIRONMENT

5.4.1 Air

Table 5-l summarizes plutonium levels measured in air at nine different locations. Since 1945, when the first nuclear weapon test at Alamogordo, New Mexico, was conducted, approximately 360 kCi (1.3×10^{16} Bq) of plutonium-239, -240 have been released into the atmosphere from various sources. The accidental burn up of the SNAP-9 satellite added 17 kCi (6.3×10^{14} Bq) to the higher altitudes of the atmosphere (Perkins and Thomas 1980).

A 15-year study (1966 to 1980) in Palomares, Spain, reported levels of plutonium in air near the site of a crash between a United States military aircraft carrying four nuclear bombs, and a tanker aircraft following the cleanup of the contaminated area (Iranzo et al. 1987).

5. POTENTIAL FOR HUMAN EXPOSURE

TABLE 5-1. Plutonium Levels Detected in Air

Location	Quantity [pCi/m^3 (Bq/m^3)]	Study	Comments
Spain, weapon accident:			
Urban area	$1.5x10^{-4}$ ($5.5x10^{-6}$) $^{239,240}Pu$	Iranzo et al. 1987	Average over 15 years
Near farm land	$1.4x10^{-3}$ ($5.2x10^{-5}$) $^{239,240}Pu$		
Savannah River Plant:			
First year:	$3.1x10^{-5}$ ($1.2x10^{-6}$) ^{238}Pu $1.5x10^{-5}$ ($4.3x10^{-7}$) $^{239,240}Pu$	Corey et al. 1982	Cumulative concentrations over one-year time period (not an average)
Second year:	$1.15x10^{-3}$ ($5.6x10^{-5}$) ^{238}Pu $3.2x10^{-5}$ ($1.2x10^{-6}$) $^{239,240}Pu$		
Rocky Flats facility:			
1 m	$2.2x10^{-3}$ (8.1x10-5) $^{239,240}Pu$	Volchok et al. 1977	Average concentrations over 7 years
1 km	$4.6x10^{-4}$ ($1.7x10^{-5}$) $^{239,240}Pu$		
2.5 km	$7.0x10^{-5}$ ($2.6x10^{-6}$) $^{239,240}Pu$		
New York City	$3.4x10^{-5}$ ($1.3x10^{-6}$) $^{239,240}Pu$	Volchok et al. 1977	Average concentrations over 7 years
New York City	$3.0x10^{-5}$ ($1.1x10^{-6}$) ^{239}Pu $1.0x10^{-5}$ ($3.7x10^{-7}$) ^{238}Pu	Hardy 1973	Typical radioactivity concentrations in ground-level air (no further specification)

Air sampling conducted continuously for 2 years (1975 to 1977) near the Savannah River Plant measured the average yearly concentrations of plutonium-238 and of plutonium-239, -240. The data for the first and second years of the study are presented in Table 5-1 (Corey et al. 1982). The data in Table 5-l indicate that releases from the Savannah River Plant and levels detected in New York City (Hardy 1973) are on the same order of magnitude and are much lower than those observed in Palomares, Spain, following the cleanup of the weapon accident. Continuous air sampling in the vicinity of the Rocky Flats facility near Denver was initiated in 1970. The data in Table 5-l are from locations 50 meters, 1 kilometer, and 2.5 km from the facility and are arithmetic means of data from sampling years 1970 to 1976. For purposes of comparison, sampling data for New York City for the same time interval are included. Data from all four locations indicated declining levels following 1971 (Volchok et al. 1977).

5.4.2 Water

Table 5-2 presents plutonium levels detected in several surface waters and groundwaters. The Pacific Ocean was sampled for plutonium and Northern Pacific concentrations were, on the average, greater than those detected in the Southern Pacific for both plutonium-239, -240 and plutonium-238 (Miyake and Sugimura 1976). The plutonium content of the particulate matter in three South Carolina estuarine systems was investigated by Hayes et al. (1976). The Neuse and Newport River estuaries received plutonium only through atmospheric fallout: the Savannah River estuary received effluent from the Savannah River Plant. Concentrations detected in the three estuaries are comparable. Raw water samples taken from three locations on the Savannah River were also found to contain levels comparable to the Savannah River estuary samples (Corey and Boni 1976). The estuarine and river concentrations were greater than the Pacific surface water samples, but were on the same order of magnitude as seawater samples taken from Trombay (Bombay, India) (Pillai and Mathew 1976). These results indicate that plutonium is found throughout the globe but that the highest concentrations of plutonium in water are found near source areas.

The groundwater at Enewetak Atoll and near the Idaho National Engineering Laboratory disposal well were found to contain plutonium-239, plutonium-240 and plutonium-238, respectively (Cleveland and Rees 1982; Noshkin et al. 1976). The isotope composition differs in the two areas (Table 5-2), and the levels detected in Idaho were, on average, lower than those detected at Enewetak Atoll. The range of groundwater concentrations at the Nevada Test Site was greater than the range detected in either of the other two groundwaters (Gonzalez 1988). Rainwater samples taken from Trombay (Bombay, India) in 1971 were reported to contain plutonium-239 concentrations greater than those

TABLE 5-2. Plutonium Levels Detected in Water

Location	Quantity pCi/L (Bq/L)	Reference
North Pacific surface water	$2.2x10^{-4}$ to $9.4x10^{-4}$ ^{238}Pu & $^{239,240}Pu$ ($8.2x10^{-6}$ to $3.5x10^{-5}$)	Miyake and Sugimura 1976
South Pacific surface water	$1.3x10^{-4}$ to $3.4x10^{-4}$ ^{238}Pu & $^{239,240}Pu$ ($4.8x10^{-6}$ to $1.3x10^{-5}$)	
Enewetak, South Pacific: Groundwater	$2.0x10^{-4}$ to $2.8x10^{-1}$ $^{239,240}Pu$ ($7.4x10^{-6}$ to $1.0x10^{-2}$)	Noshkin et al. 1976
Idaho National Engineering Laboratory: Groundwater	$1.1x10^{-2}$ to $7.8x10^{-2}$ ^{238}Pu ($4.1x10^{-4}$ to $2.9x10^{-3}$)	Cleveland and Rees 1982
South Carolina:		
Estuarian waters	$1.7x10^{-4}$ to $2.5x10^{-3}$ $^{239,240}Pu$ ($6.3x10^{-6}$ to $9.4x10^{-5}$)	Hayes et al. 1976
River waters	$4.3x10^{-4}$ to $2.3x10^{-3}$ $^{239,240}Pu$ ($1.6x10^{-5}$ to $8.3x10^{-5}$)	Corey and Boni 1976
Trombay, India:		
Rainwater	$8.2x10^{-2}$ ($3.0x10^{-3}$) ^{239}Pu $4x10^{-3}$ to $2x10^{-2}$ ^{239}Pu ($1.5x10^{-4}$ to $7.4x10^{-4}$)	Pillai and Mathew 1976
New York City:		
Drinking water	$8x10^{-5}$ to $6.1x10^{-4}$ $^{239,240}Pu$ ($3.0x10^{-6}$ to $2.3x10^{-5}$)	Bogen et al. 1988
Nevada Test Site:		
Groundwater	$4.2x10^{-2}$ to 2.6 ^{239}Pu ($1.6x10^{-3}$ to $9.6x10^{-2}$)	Gonzalez 1988

detected in seawater from the same area, as seen in Table 5-2 (Pillai and Mathew 1976).

Plutonium concentrations in the New York water supply measured between 1974 and 1979 showed a peak concentration of plutonium-239, -240 in the summer of 1974 which fell within the range of other surface waters analyzed (Table 5-2). The low concentration detected during the following autumn was below the concentrations detected in other waters (Bogen et al. 1988).

5.4.3 Soil

Average fallout levels in soils in the temperate United States are about 2,100,000 pCi/km^2 ($7.8x10^4$ Bq/km^2) plutonium-239, -240 and 50,000 pCi/km^2 ($1.9x10^3$ Bq/km^2) plutonium-238 (Hanson 1975). Mean deposition rates of stack-released plutonium-238 to soils around the Savannah River Plant range from 0.008 to 0.64 pCi/m^2/day ($3.0x10^{-4}$ to $2.4x10^{-2}$ Bq/m^2/day) . The range for plutonium-239, -240 was found to be 0.027 to 0.36 pCi/m^2/day ($1.0x10^{-3}$ to $1.33x10^{-2}$ Bq/m^2/day). The lower concentrations were measured 9 km from the plant and the higher concentrations were measured 0.23 km from the plant (Corey et al. 1982).

Plutonium levels in soils at Rocky Flats, Colorado, were analyzed by Little and Whicker (1978). Plutonium concentrations in soil samples collected to a depth of 21 cm had plutonium concentrations ranging from 1,400 to 59,000 pCi/kg (52 to 2,200 Bq/kg). A recent study on particle size and radionuclide levels in Great Britain soils reported plutonium-238 levels detected at a range of 200 to 18,000 pCi/kg (7.4 to 676 Bq/kg) and plutonium-239, -240 levels detected at a range of 800 to 83,000 pCi/kg (29.6 to 3,070 Bq/kg) (Livens and Baxter 1988). Core samples of surface soil at the Maxey Flats facility, where radioactive wastes were buried, were reported to contain a mean concentration of $1.9x10^5$ pCi/kg (67 Bq/kg) of plutonium-238 and 22,000 pCi/kg (8 Bq/kg) of plutonium-239 and plutonium-240 (NEA/OECD 1981).

Plutonium concentrations found in Lake Michigan sediments were reported to range from 35 to 250 pCi/kg dry sediment ($9.5x10^{-22}$ to $6.8x10^{-21}$ Bq/kg) (Edgington et al. 1976). It was estimated in this report that radioactivity in the sediments was confined to the upper 6 cm of the sediments, and in many of the core samples, no radioactivity was detected below a depth of 3 cm.

5.4.4 Other Media

A 1972 study on plutonium levels in the diet reported concentrations of plutonium-239, -240 ranging from $<2x10^{-7}$ pCi/g ($<7.4x10^{-9}$ Bq/g) for canned fruit to $1.1x10^{-4}$ pCi/g ($4.1x10^{-6}$ Bq/g) in shellfish (Bennett 1976b). Of the shellfish sampled in this report (clams and shrimp), clams showed eight times the levels of plutonium

found in shrimp. Fish and shellfish sampled in the Windscale and Northeast areas of the Irish Sea were reported to contain between 2.0×10^{-4} pCi/g (7.4×10^{-6} Bq/g) (herring muscle) and 2 pCi/g (0.074 Bq/g) (soft parts of mussel) (Hetherington et al. 1976).

5.5 GENERAL POPULATION AND OCCUPATIONAL EXPOSURE

Daily ingestion of plutonium-239, -240 in food in Japan between 1978 and 1980 due to atmospheric fallout was estimated to be 0.0045 pCi/day (1.7×10^{-4} Bq/day) (Hisamatsu et al. 1987). In 1974, the mean intake of plutonium in New York City from all sources including tap water was reported to be 0.0044 pCi/day (1.6×10^{-4} Bq/day) (Bogen et al. 1988). This same value was reported for daily intakes of plutonium in Italy from 1975 to 1978 (Bennett 1976b). Ingested plutonium is poorly absorbed from the gastrointestinal tract, although the form of plutonium will influence absorption (ICRP 1982).

The isotope of plutonium inhaled will affect its behavior in the body. The bones and the liver are the primary organs for plutonium deposition following translocation in the body (ICRP 1982). However, McInroy et al. (1989) indicate that muscle tissue may also be a site of deposition. Plutonium-238 dioxide is more rapidly translocated from the lungs than plutonium-239 dioxide thereby causing more plutonium-238 to be concentrated in other body tissues (ICRP 1982).

Mean concentrations of plutonium-239, -240 in human tissues from autopsy specimens in Japan ranged from 0.00025 pCi/g (9.3×10^{-6} Bq/g) (cerebrum) to 0.0015 pCi/g (5.4×10^{-5} Bq/g) (gonads) fresh weight (Takizawa 1982).

Wrenn and Cohen (1977) reported plutonium-239 levels in tissues derived from 12 autopsy cases in New York City from 1973 to 1976. Average levels for lung, liver, vertebrae, and gonads were 0.00024 pCi/g of tissue (8.9×10^{-6} Bq/g), 0.0007 pCi/g (2.6×10^{-5} Bq/g), 0.00017 pCi/g (6.3×10^{-6} Bq/g), and 0.0004 pCi/g (1.5×10^{-5} Bq/g), respectively.

Tissue samples from autopsy cases of nonoccupationally exposed individuals from Great Britain showed median plutonium-239, -240 levels for ribs, vertebrae, femur, liver and lungs of 0.00016 pCi/g (5.9×10^{-6} Bq/g), 0.00012 pCi/g (4.4×10^{-6} Bq/g), 0.000095 pCi/g (3.5×10^{-6} Bq/g), 0.0007 pCi/g (2.6×10^{-5} Bq/g) and 0.000049 pCi/g (1.8×10^{-6} Bq/g), respectively. Comparable samples taken from autopsy cases from a region in Great Britain located near a plutonium processing plant had median concentrations of 0.00022 pCi/g (8.1×10^{-6} Bq/g), 0.00019 pCi/g (7.0×10^{-6} Bq/g), 0.00015 pCi/g (5.6×10^{-6} Bq/g), 0.00014 pCi/g (5.2×10^{-5} Bq/g) and 0.00018 pCi/g (6.7x10-6 Bq/g) for those tissues mentioned above (Popplewell et al. 1988).

The estimated 50-year dose commitment from plutonium for people in the north temperate zone due to atmospheric tests conducted before 1973 is 0.2 mrad (0.002 mGy) to the bone lining cells (Eisenbud 1987). [The gray is an SI unit of absorbed dose and is equal to 0.01 rad.] The average annual dose equivalent from all background radiation to an individual residing in the United States is estimated to be 360 mrem (3.6 mSv**)** (NCRP 1987). [The sievert is an SI unit of dose equivalent and is equal to 0.01 rem.]

5.6 POPULATIONS WITH POTENTIALLY HIGH EXPOSURES

Individuals employed at facilities using plutonium or uranium have high exposure potentials. Voelz et al. (1985) studied workers who participated in the Manhattan Project to determine if they had been exposed to levels of plutonium which would result in adverse health effects. Examination of the study group showed that their health was as good, if not better, than the general population. Similar results were reported by Wilkinson et al. (1987) for individuals employed at a plutonium weapons facility. These authors found, however, that individuals with body burdens $\geq$2,000 pCi ($\geq$74 Bq) had **a** slightly higher mortality from all causes of death and from lymphopoietic neoplasms than that found in employees with body burdens <2,000 pCi (<74 Bq). (See Section 2.2.1.8 for a more complete discussion of this study.)

Cobb et al. (1982) obtained autopsy tissues from individuals who had lived in one of three areas around the Rocky Flats facility (449 decedents) and from individuals who had lived outside of these areas for use as control data. Total plutonium burden, as well as the ratio of plutonium-239, -240, were measured in lung and liver tissues from these individuals. Next of kin were interviewed to assure that none of the study population had been exposed to plutonium from sources other than fallout and/or environmental contamination from the Rocky Flats facility, and to obtain information on smoking history. Multiple regression analyses suggested that plutonium burden is related to age, sex, and smoking history, but showed no definitive relationship to residence near the Rocky Flats facility. The correlation of plutonium burden with smoking (measured in pack-years) indicated that smokers could be a population at risk for increased body burden. The authors of the study hypothesize that this may result from damage to the clearing mechanisms of the lungs, resulting in a decrease in the rate of natural elimination of particles.

Individuals living near facilities which utilize plutonium in the operations may have higher exposure potential due to regular releases through stack-emissions or waste water. In addition, atmospheric fallout to the soil can result in secondary releases due to dust generation while farming or due to uptake by crops and subsequent ingestion of contaminated crops (Corey et al. 1982).

Individuals living in Palomares, Spain, were exposed to plutonium after the dispersal of the plutonium in two bombs released during the midair collision of two airplanes (Iranzo et al. 1987). Exposure via inhalation due to the resuspension of contaminated soil was studied for 15 years following the release. Those individuals living near cultivated lands with the highest contamination received a cumulative total of 52.3 mrem (5.2×10^{-1} mSv) from 1966 to 1980 while those in the urban area of Palomares, farther away from the source, received 5.4 mrem (5.4×10^{-2} mSv) (Iranzo et al. 1987).

Kathren et al. (1987) determined levels of plutonium-239 at autopsy in bones of an individual known to have had occupational exposure to plutonium. Values ranged from 1.9×10^{-4} to 1.14×10^{-2} pCi/g ash (7.0×10^{-6} to 5.0×10^{-5} Bq/g ash), with the highest value detected in the scapula. Kathren et al. (1988) found a greater percentage of plutonium-238 in the skeleton than plutonium-239.

Kawamura (1987) estimated the plutonium-239, -240 inhalation intake of visitors to Kiev after the Chernobyl accident to be 0.8 pCi/day (0.03 Bq/day) during peak fallout exposure.

5.7 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of plutonium is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of plutonium.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met would reduce or eliminate the uncertainties of human health assessment. In the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

5.7.1 Identification of Data Needs

Physical and Chemical Properties. The physical and chemical properties of plutonium have been studied. The information is adequate to permit estimation of plutonium's environmental fate.

Production, Use, Release, and Disposal. The potential for human exposure to plutonium is great due to its ubiquitous presence in the environment, resulting from releases from production facilities and from

weapons testing, and its radiological half-life. However, the level of exposure to plutonium may be small. The production and use of plutonium 238-243 are well documented. There is little information regarding the production of plutonium-237. The amounts of these plutonium isotopes produced for various applications have been documented; however, the most current information is from 1974. More recent data is needed in order to compare past and present production and to project future production. The majority of information on the production and use of plutonium is classified in the nation's defense program. Information on past major releases of plutonium from weapons testing and from the explosion of a navigational satellite is available. However, current information on releases from production facilities is unavailable and is needed in order to monitor populations that might be exposed. The disposal of plutonium prior to 1970 is documented, but again, more recent information regarding amounts being held for mandated disposal in the proposed high-level disposal facility is needed. Rules and regulations for the disposal of plutonium have been established and these are reported in Chapter 7.

Environmental Fate. The major transport processes involved in the environmental fate of plutonium, as it relates to potential human exposure, have been fairly well defined. These processes include transport in the atmosphere when adsorbed to particulate matter and dry or wet deposition on land and water. Information on environmental compartments, such as flux rates, and the mechanisms and rates of several processes involved in the biogeochemical cycling of plutonium are still undefined. The data available regarding uptake of plutonium by plants are limited. There is some information regarding the conversion of the oxidized forms of plutonium to reduced forms followed by uptake into plants. Information regarding the influence of inorganic complexes on transport and regarding the media-specific effects of pH on the oxidation states of plutonium would be useful in order to more fully understand transport processes. The persistence of plutonium isotopes is well documented. Transformation of plutonium is through radioactive decay or chemical oxidation/reduction reactions. These processes have been well characterized.

Bioavailability. Plutonium is known to be absorbed following inhalation exposure. Bioavailability following oral and dermal exposure is very low; however, plutonium can be absorbed from contaminated wounds. Bioassay data are available on absorption from contaminated air and water. However, information on the impact of the valence state of plutonium on absorption following oral exposure is ambivalent. Such information is needed in order to address the impact of chlorination of drinking water, which results in a change in the valence of plutonium from plutonium(IV) to plutonium(V1). Therefore, further testing is important to determine the relevance of this change in valence state. No data were located on absorption from ingestion of soil or plant

material. Such information is needed in order to quantify the potentiail exposure by this route, particularly when children may ingest soil when playing near NPL sites.

Food Chain Bioaccumulation. Plutonium has been shown to bioconcentrate in aquatic organisms at the lower end of the food chain. However, data do not indicate that plutonium is bioconcentrated in plants, higher aquatic organisms, or animals. In addition, there is no indication that plutonium is biomagnified in terrestrial or aquatic food chains. No additional information on bioaccumulation appears to be necessary at this time.

Exposure Levels in Environmental Media. A number of studies have been performed throughout the years on the fallout associated with the testing of nuclear weapons. Information is available on levels in air, water, soil, plant materials, and foodstuffs. However, no recent data are available on levels in these media. In particular, information is very limited on levels in media associated with areas surrounding waste sites. Such information is needed in order to quantify the potential exposure via these sources. Data are not available on estimates of human intake via specific media. This information would be important in determining the impact of exposure through each of these media.

Exposure Levels in Humans. Plutonium is measurable in urine and in lung, liver, and bone tissues obtained from autopsy. It is plausible to expect that occupationally exposed populations are routinely biomonitored through urinalysis. However, such data are not made available and are needed to quantify exposure to these individuals. In addition, no information is available on biomonitoring of individuals around NPL sites where plutonium has been found or of the general public. This information is needed so that exposure to these populations may be quantified.

Exposure Registries. No exposure registries for persons environmentally exposed to plutonium were located. Plutonium is not currently one of the substances for which a subregistry has been established in the National Exposure Registry. The substance will be considered in the future when chemical selection is made for subregistries to be established. The information that is amassed in the National Exposure Registry facilitates the epidemiological research needed to assess adverse health outcomes that may be related to the exposure to this substance.

5.7.2 On-going Studies

Long-term research studies on the environmental fate of plutonium have not been identified. However, with the Chernobyl accident, it is

anticipated that new information regarding the transport and fate of materials released during the accident will become available.

N.P. Singh (University of Utah) is determining the concentration and accumulation of plutonium in different organs of the younger population of the United States, who were born after 1963. Another study includes determining the concentrations of plutonium-238, plutonium-239, and plutonium-240 in the liver, kidney, and bone of 30 people who lived in northern Utah.

C.R. Olsen (Oak Ridge National Laboratory), along with other researchers, is investigating whether radionuclides released from the Department of Energy Savannah River facilities might be useful environmental tracers. The study includes transport pathways, transfer rates, and geochemical fate of plutonium in the Savannah River estuary. R.E. Wildung at Pacific Northwest Laboratory is studying the influence of soil, soil microbial, and plant processes on behavior and cycling of cationic elements (including plutonium) in terrestrial environments.

The behavior of long-lived radionuclides in natural water (W.R. Penrose, Argonne National Laboratory) and the behavior of falloutderived plutonium in estuarine sediments as a function of various environmental parameters (H.J. Simpson, Columbia University) have been under investigation. The study by Simpson includes determining factors which control the distribution of plutonium in the sediments of the Hudson River. Studies by Noshkin and Penrose include characterizing rates and mechanisms of various physical and chemical processes that control the behavior of such pollutants, and characterizing the importance of oxidation states and natural complexing agents on the sorption behavior of plutonium and other radionuclides.

Geochemistry of plutonium in the Gulf of Mexico is being studied by M.R. Scott (Texas A&M University). Plutonium isotopes will be measured in both oxic and anoxic sediments in the Gulf of Mexico and in suspended sediments from major rivers emptying into the Gulf.

G.R. Choppin (Florida State University) is investigating the synergistic reaction of actinide-TTA complexes with brown ether adducts in benzene solutions and interaction of plutonium and other transuranic elements with the components of marine sediments under different conditions. The interaction of plutonium-238 dioxide heat source with the marine environment is also under investigation by H.V. Weiss (Naval Coastal Systems Center).

6. ANALYTICAL METHODS

The purpose of this chapter is to describe the analytical methods that are available for detecting and/or measuring and monitoring plutonium in environmental media and in biological samples. The intent is not to provide an exhaustive list of analytical methods that could be used to detect and quantify plutonium. Rather, the intention is to identify well-established methods that are used as the standard methods of analysis. Many of the analytical methods used to detect plutonium in environmental samples are the methods approved by federal agencies such as EPA. Other methods presented in this chapter are those that are approved trade associations, such as the Association of Official Analytical Chemists (AOAC) and the American Public Health Association (APHA). Additionally, analytical methods are included that refine previously used methods to obtain lower detection limits and/or to improve accuracy and precision.

The accurate and reliable determination of plutonium in biological and environmental samples is important because of the potential impact of this element on public health. Analytical methods used to measure plutonium in biological and environmental media are highly refined compared to other transuranics.

Analytical methods used to quantify plutonium in biological and environmental samples are listed in Tables 6-l and 6-2. Emphasis has been placed on well-established methods approved by EPA, the American Public Health Association, and in accordance with accepted standards of the American Society for Testing and Materials (ASTM). Reviews of analytical methods for measuring plutonium concentrations are provided by Brouns (1980), Bernhardt (1976), Metz and Waterbury (1962), and Singh and Wrenn (1988).

General environmental survey instruments (e.g., alpha particle meters) are available, but they are not specific for plutonium. The predominant analytical method for measuring plutonium present at or near background concentrations in both biological and environmental media requires radiochemical separation and purification in conjunction with a quantitative measurement technique (e.g., alpha spectrometry, liquid scintillation, or mass spectrometry).

6.1 BIOLOGICAL MATERIALS

The procedures that have been developed for the determination of small quantities of plutonium in biological as well as in environmental samples include the following steps:

- Release of plutonium from the sample's matrix into solution and the addition of plutonium tracers;

TABLE 6-1. Analytical Methods for Determining Plutonium in Biological Materials

Sample Matrix	Sample Preparation	Analytical Method	Sample Detection Limit	Accuracy	Reference
Biological soft tissues	Wet ash; filter; extract; electrodeposit on platinum disk	α spectrometry ^{238}Pu, $^{239/240}Pu$	no data	no data	Singh and Wrenn 1988
Urine	Evaporate; wet ask; filter; extract, electro-deposit on platinum disk	α spectrometry ^{238}Pu, $^{239/240}Pu$	no data	no data	Singh and Wrenn 1988
Fecal matter	Wet ash; filter; extract; electrodeposit on platinum disk	α spectrometry ^{238}Pu, $^{239/240}Pu$	no data	no data	Singh and Wrenn 1988
Bones	Dry ash; reduce valence state; extract; electrodeposit on platinum disk	α spectrometry ^{238}Pu, $^{239/240}Pu$	no data	no data	Singh and Wrenn 1988
Milk	Dry ash; extract; reduce valence state; coprecipitate with lanthanum fluoride	α spectrometry	no data	no data	EPA 1984
Plant	Dissolve starch; filter; wet ash; extract; electrodeposit on platinum disk	α spectrometry ^{238}Pu, $^{239/240}Pu$	0.0027 pCi ($0.1x10^{-4}$ Bq)	no data	Bunzl and Kracke 1987

TABLE 6-2. Analytical Methods for Determining Plutonium in Environmental Samples

Sample Matrix	Sample Preparation	Analytical Method	Sample Detection Limit	Accuracy	Reference
Air	Extract; filter; coprecipitate with cerium fluorides; electrodeposit on platinum disk	α spectrometry (solid state detector) (tentative Method 605)	0.08×10^{-6} pCi/m^3 (2×10^{-6} Bq/m^3)	±10%	APHA 1977
Air	Dry ash; filter; extract; reduce valence; coprecipitate with lanthanum fluoride	α spectrometry	no data	no data	EPA 1984
Soil	Digest; filter; extract; electrodeposit on platinum disk	α spectrometry ^{238}Pu, $^{239/240}$Pu	no data	no data	Singh and Wrenn 1988
Soil, Water	Ash soil or evaporate water samples; reduce valance; extract; wet ash; coprecipitate with lanthanum fluoride	α spectrometry ^{238}Pu, $^{238/240}$Pu	no data	no data	EPA 1984
Water	Filter; extract; coprecipitate with lanthanum fluoride	α particle counter (either proportional or scintillation detectors) (EPA Method 907.0)	no data	15%	EPA 1980

6. ANALYTICAL METHODS

- Concentration by precipitation with a nonisotopic carrier or by solvent extraction;
- Purification by precipitation, liquid extraction, or ion exchange chromatography; and
- Determination of the plutonium content of the sample by alpha-particle counting or other techniques (Brouns 1980).

Two common methods for releasing plutonium from the sample's matrix into solution are acid extraction and acid dissolution. Samples are wet, or dry, ashed prior to solubilization. Leaching the sample with a mixture of acids (e.g., nitric acid and hydrochloric acid) has the advantage of easily handling large sample volumes, but with the potential disadvantage of leaving plutonium compounds in the residue. The acid dissolution procedure includes the addition of excess hydrofluoric acid (HF) to the above mixture of acids and results in dissolution of much, if not all, of the sample matrix. Refractory plutonium compounds (e.g., PuO_2,) are more likely to be dissolved upon addition of HF. However, dissolution of interfering elements, such as iron, phosphorous, and other rare earths (e.g., alpha-particle emitters), is also increased in acid dissolution. A third example of a dissolution method is fusion. It is less routinely used, however, because it is relatively labor intensive. Fusions with pyrosulfate, or a combination potassium fluoride and pyrosulfate fusion, can insure complete dissolution of the sample matrix. The potassium fluoride fusion dissolves the siliceous material in the sample, whereas the pyrosulfate fusion dissolves the nonsiliceous matrix materials, especially the refractory plutonium dioxides (Bernhardt 1976).

Plutonium solutions that contain: (1) other alpha-particle emitters (e.g, americium and neptunium), (2) large amounts of fission products (e.g., cesium), or interfering amounts of other substances such as iron, calcium, uranium, and phosphorous need to undergo additional chemical separation procedures. Nonisotopic carriers, such as lanthanum fluoride (LaF_3) and zirconium phenylphosphate ($ZrC_6H_6PO_4$), are used to selectively precipitate the rare earths. Solvent extraction and ion exchange separation methods are preferred methods because of better separations. In addition, they do not involve the addition of nonvolatile substances resulting in an easier preparation of the co-precipitation source used for alpha-particle counting.

These extraction techniques can be made very efficient and selective by adjusting the oxidation state of the plutonium and other sample constituents. Common extraction methods specific for plutonium use 2-thenoyltrifluoroacetone (TTA), tetrapropylammonium trinitrate in isopropylacetone or triisooctylamine, cupferron in chloroform, tributylphoshphate, and tri-octylphosphine dioxide. Anion exchange

methods with either nitric or hydrochloric acid solutions are commonly used. Cation exchange column methods are less frequently used (Brouns 1980).

Alpha-particle counting is the most commonly used method for determining plutonium concentrations at low levels in biological samples, as well as in process waste streams, and in soil, water, and air filter samples (Brouns 1980). This method does not distinguish between the different alpha-particle emitters of plutonium (plutonium-236, plutonium-238, plutonium-239, plutonium-240, plutonium-242), nor does it detect plutonium-241, a beta-particle emitter.

Prior to measurement, the separated and purified plutonium must be incorporated into a source to produce a low mass, uniformly distributed deposit on a highly polished metal surface. Two techniques that are commonly used are: (1) electrodeposition, and (2) co-precipitation with a carrier. Electrodeposition is currently used in a minority of laboratories to prepare a thin, uniform, and reproducible source. The alpha-particle emitting isotopes of plutonium are electrodeposited on a polished stainless steel, or platinum disk. In the co-precipitation technique, a small amount of a carrier (e.g., LaF3) is used to coprecipitate the separated and purified plutonium from solution. The precipitate is then prepared for counting by either filtration or by evaporation of a slurry of the precipitate onto a stainless steel disk or planchet (ASTM 1982; 1987). Recent methods use a glass fiber filter which can be used as the source for alpha counting techniques. It has been suggested that low yields result from electrodeposition due to the presence of traces of interfering elements (e.g., iron) (Bernhardt 1976).

Alpha spectrometry is the single most widely used method for measuring concentrations of plutonium-238, or a mixture of plutonium-239 and plutonium-240. However, the energy of the alpha particles emitted from plutonium-239 and plutonium-240 are too close to be resolved by alpha spectrometry. The two remaining alpha-particle emitters among the plutonium isotopes, plutonium-236 and plutonium-242, are normally not found in environmentally significant quantities, and are not common constituents of nuclear fuels or waste waters. Therefore, they can be used as tracers to aid in the analysis of other isotopes. In this calibration procedure, a known quantity of a tracer is added to the sample being analyzed in order to determine the yield. This is the percentage of the total amount of plutonium in the sample that is actually measured in the electrodeposited amount after the separation, purification, and preparation of the source (ASTM 1987; Brouns 1980).

The most critical step in the analysis of biological samples is complete dissolution of the sample to assure solubilization of all plutonium compounds. Biological samples are generally dissolved by wet ashing or a combination of wet and dry ashing. High temperatures (700%

to 1,000°C) during ashing should be avoided in order to prevent the formation of an insoluble form of plutonium dioxide (Nielsen and Beasley 1980; Sill 1975). Plutonium that has been distributed to urine, blood, or soft tissue as a result of metabolic processes is usually in a readily soluble form. Lung tissue, feces, and excised tissue from wound sites will likely contain insoluble forms of plutonium and will require treatment with HF and repeated ashings to effect solubilization. Tissues, feces, and vegetation require repeated treatment wit'n a mixture of concentrated nitric acid (HNO,), perchloric acid ($HC10_4$,), and sulphuric acid (H_2SO_4) in order to oxidize the large amount of organic materials in these samples. If an insoluble residue remains after repeated ashings, then fusion of the residue with gram quantities of an inorganic flux (e.g., sodium carbonate, sodium pyrosulfate) can be used to effect solution. Known amounts of a plutonium isotope are commonly added subsequent to the dissolution step so that the percentage of plutonium recovered after separation and purification (i.e., the yield) may be determined. This added plutonium must be in the same chemical form as the plutonium in the sample or the yield estimates will not reflect the percentage of plutonium recovered from the dissolved sample (Bernhardt 1976; Nielsen and Beasley 1980).

Methods used for concentrating plutonium in a sample by a carrier are often specific to one oxidation state of the plutonium. For example, the classical bismuth phosphate-lanthanum fluoride method of concentrating plutonium from urine samples is specific to plutonium in the tri- and tetravalent states and will leave plutonium(V1) in solution. The fate of the various oxidation states of plutonium in man is not well understood and analysis procedures must insure reduction or oxidation of plutonium into appropriate oxidation states. Liver and kidney samples may contain metals (e.g., iron) which may greatly reduce chemical yields during the final electrodeposition step (Bernhardt 1976).

Sensitive methods for analysis of plutonium in urine are particularly important for estimating occupational plutonium body burdens. Routinely available instrumentation, such as the alpha spectrometer, can readily detect these low concentrations. More sensitive methods are commonly required for urine samples in order to assess chronic exposures to plutonium. These low detection limits were first achieved in the past by nuclear emulsion track counting (see Table 6-l). In this method, the electrodeposited sample is exposed to nuclear track film, subsequent to the isolation of plutonium. The alphaparticle emitting isotopes of plutonium will leave tracks on the film which are counted to quantify the amount of plutonium. Nuclear emulsion track counting has been used in the past to measure plutonium concentrations in the urine of workers at a nuclear reactor plant (Nielsen and Beasley 1980). A type of scintillation counting has been used to measure plutonium-239 and americium-241 in animal tissues (NCRP 1985).

6.2 ENVIRONMENTAL SAMPLES

Common analytical methods used to measure plutonium in environmental samples are listed in Table 6-2. The separation and extraction methods used to prepare biological samples for plutonium analysis are commonly used for environmental samples.

Large volumes of air particulate samples (e.g., 10,000 m^3) should be collected in order to obtain detectable amounts of plutonium. Fiberglass filters may have trace amounts of metals which decrease the yield when electroplating is used to prepare the sample source for alpha spectrometry (Bernhardt 1976).

Field survey instruments for measuring photons of americium-241 in surface soils and on airborne particulates are available (e.g., Field Instrument for Detecting Low Energy Radiation: FIDLER) with a minimum detection limit of approximately twice the magnitude of a background level of plutonium-239 ($1\text{-}2x10^3$ pCi/m^2; 37-74 Bq/m^2). The FIDLER uses a sodium iodide or calcium fluoride crystal and photon-height discrimination in order to detect the 17 KeV X-rays emitted from the progeny of plutonium, or the 60 KeV gamma photons of americium-241. These instruments are useful for identifying areas of contamination, but cannot be used to accurately predict the concentration of plutonium in surface soils (Bernhardt 1976). This instrument has been used in aerial surveys of large area sources, such as the Nevada Test Site.

Since soil-adsorbed plutonium contamination exists as discrete particles of various sizes, analysis of larger soil volumes (25 to 100 grams) is recommended (Bernhardt 1976). Commonly, soil samples with high amounts of carbonate are difficult to analyze. More rapid, efficient, and economical procedures are being developed to sequentially analyze a number of radioactive actinides (Hindman 1986).

An EPA-approved procedure for the analysis of plutonium in water is listed in Table 6-2. In addition, the following ASTM standard methods relate to the measurement of plutonium in water: D 3648, D 3084, D 3972, and D 1943 (ASTM 1981, 1982a, 1982b, 1987). Recent work has focused on more rapid analytical methods in order to routinely monitor plutonium levels in waste process streams at nuclear facilities. For example, Edelson et al. (1986) have investigated the applications of inductivelycoupled lasma-atomic emission spectrometry (ICP-EAS) to routinely analyze water samples.

Alpha counting and alpha spectrometry are the two most common analytical methods for measuring plutonium concentrations in environmental samples. Other measurement techniques available are liquid scintillation, mass spectrometry, and gamma spectrometry.

Liquid-scintillation counting is a less common method used to measure plutonium concentrations from the various alpha-particle emitters among the isotopes of plutonium. Although liquid scintillation counting avoids the interferences from iron and other metals seen with electrodeposition, this method generally has higher detection limits than obtained with alpha spectrometry. In addition, the composition of the scintillation solution must be carefully controlled to prevent polymerization, deposition, or precipitation of the plutonium (NCRP 1985).

Mass spectrometry is used by some research laboratories to determine the concentration of each plutonium isotope, including the naturally-occurring plutonium-244. Mass spectrometry determines the number of atoms of a given mass number and, therefore, can measure the concentration of all of the plutonium isotopes, not only the aiphaparticle emitters as in alpha spectrometry. Mass spectrometry is several orders of magnitude more sensitive than alpha spectrometry in determining the quantities of plutonium isotopes with long half-lives, which also tend to be the heavier isotopes. However, plutonium-238 is most accurately determined by alpha spectrometry (Bernhardt 1976) because of its relatively short half-life and the potential interferences from traces of uranium-238.

Quantities of plutonium-241, a beta-particle emitter, can be quantified from: (1) assumed isotopic abundance ratios, (2) estimated in-growth of its progeny americium-241 by gamma spectrometry, or by (3) mass spectrometry (Bernhardt 1976). Americium-241 is produced from the beta decay of plutonium-241 and, therefore, can be used to indirectly measure the concentration of plutonium-241 (Metz and Waterbury 1962). Direct determination of plutonium-241 by measurement of its low energy beta-particle decay has been reported using liquid scintillation analysis (Martin 1986).

6.3 ADEQUACY OF THE DATABASE

Section 104(i)(5) of CERCLA, directs the Administrator of ATSDR (in consultation with the Administrator of EPA and agencies and programs of the Public Health Service) to assess whether adequate information on the health effects of plutonium is available. Where adequate information is not available, ATSDR, in conjunction with the NTP, is required to assure the initiation of a program of research designed to determine the health effects (and techniques for developing methods to determine such health effects) of plutonium.

The following categories of possible data needs have been identified by a joint team of scientists from ATSDR, NTP, and EPA. They are defined as substance-specific informational needs that, if met would reduce or eliminate the uncertainties of human health assessment. In

the future, the identified data needs will be evaluated and prioritized, and a substance-specific research agenda will be proposed.

6.3.1 Identification of Data Needs

Methods for Determining Biomarkers of Exposure and Effect. There are methods available for measuring the isotopes of plutonium in biological samples. The measurement of plutonium in the urine is considered a biomarker of exposure to plutonium. Methods are available to detect plutonium in the urine. However, no information was available concerning the reliability of these methods for determining plutonium levels in the urine. In the studies that reported these methods of analyses, neither the sample detection limit nor the accuracy of the method was reported. Therefore, more information is needed to define a detection limit and to determine the accuracy of the method used to analyze plutonium in the urine. On-going studies continue to refine these procedures. Additional studies would be helpful to determine the migration of plutonium in the body over time.

No biomarkers have been linked to plutonium health effects in humans. Further testing to identify any potential biomarkers of effect should be conducted; if biomarkers are identified, testing will then be needed to determine what analytical methods will detect these biomarkers with the greatest degree of accuracy.

Methods for Determining Parent Compounds and Degradation Products in Environmental Media. Environmental media are analyzed to identify contaminated areas and to determine if contaminant levels constitute a concern for human health. The detection of plutonium in air, water, and soil is of concern due to the potential for human exposure. There are many steps involved in the analysis of plutonium in environmental media. Reliable and accurate methods are available to detect plutonium in air. However, no detection limit or degree of accuracy was reported for the methods used to determine plutonium in soil and water. Attempts to improve these methods should be focused on separation techniques, increasing yields, and increasing the measurement efficiency.

6.3.2 On-going Studies

The Environmental Research Laboratory of the U.S. Department of Energy located in New York is conducting studies to refine analytical methods for the measurement of plutonium in biological and environmental media. Lawrence Livermore National Laboratory in California is currently refining techniques for the measurement of plutonium in biological samples. On-going studies of the solution chemistry of plutonium are currently being undertaken at Brookhaven Laboratory in New York and by researchers in Japan (Aoyagi et al. 1987).

6. ANALYTICAL METHODS

Individuals occupationally exposed to plutonium in the past are continually monitored in programs across the country. For example, whole body counting studies are currently conducted at Los Alamos National Laboratory in New Mexico. Animal studies conducted at the Lawrence Berkeley Laboratory, University of California, Berkeley, by P. Durbin are evaluating the behavior and movement of plutonium inhaled into the lungs. Models used to estimate body burden based on urinary excretion data and other biological measurements of plutonium (Leggett and Eckerman 1987) are under continual revision.

7. REGULATIONS AND ADVISORIES

International and national regulations and guidelines pertinent to human exposure to plutonium and to other radioactive substances are summarized in Table 7-l. Recommendations for radiation protection for people in the general population as a result of exposure to radiation in the environment are found in the Federal Radiation Guidance (FRC 1960) and ICRP No. 26 (ICRP 1977). National guidelines for occupational radiation protection are found in the "Federal Radiation Protection Guidance for Occupational Exposure" (EPA 1987). This guidance for occupational exposure supersedes recommendations of the Federal Radiation Council for occupational exposure (FRC 1960). The new guidance presents general principles for the radiation protection of workers and specifies the numerical primary guides for limiting occupational exposure. These recommendations are consistent with the ICRP (ICRP 1977).

The basic philosophy of radiation protection is the concept of ALARA (As Low As Reasonably Achievable). As a rule, all exposure should be kept as low as reasonably achievable and the regulations and guidelines are meant to give an upper limit to exposure. Based on the primary guides (EPA 1987), guides for Annual Limits on Intake (ALIs) and Derived Air Concentrations (DACS) have been calculated (ICRP 1977, 1979). The AL1 is defined as "that activity of a radionuclide which, if inhaled or ingested by Reference Man (ICRP 1975), will result in a dose equal to the most limiting primary guide for committed dose" (EPA 1988a) (see Appendix B). The DAC is defined as "the concentration of radionuclide in air which, if breathed by Reference Man (ICRP 1975) for a work-year, would result in the intake of one ALI" (EPA 1988a). The ALIs and DACs refer to occupational situations but may be converted to apply to exposure of persons in the general population by application of conversion factors (Table 7-l).

7. REGULATIONS AND ADVISORIES

TABLE 7-1. Regulations and Guidelines Applicable to Plutonium and Plutonium Compounds

Agency	Description	Value*	References
	<u>International</u>		
Guidelines:			
ICRP	Occupational - whole body exposure	5 rem/yr (50 mSv)	ICRP 1977
ICRP	Individual - short-term, to critical populations	0.5 rem/yr (5 mSv)	ICRP 1977
ICRP	Individual - chronic exposure	0.1 rem/yr (1 mSv)	ICRP 1977
	<u>National</u>		
Regulations:			
a: Air:			
NRC	Cumulative annual dose limit for general population from nuclear power plant operations	0.5 rem/yr	NRC 1988[a] 10 CFR 20.105(a)
NRC	Maximum concentration above background released at the boundary of power plant:	<u>pCi/ml (Bq/ml)</u>	NRC 1988[a] 10 CFR 20.106(a)
	Plutonium-238 S	7×10^{-8} (3×10^{-9})	
	I	1×10^{-6} (4×10^{-8})	
	Plutonium-239 S	6×10^{-8} (2×10^{-9})	
	I	1×10^{-6} (4×10^{-8})	
	Plutonium-240 S	6×10^{-8} (2×10^{-9})	
	I	1×10^{-6} (4×10^{-8})	
	Plutonium-241 S	3×10^{-6} (1×10^{-7})	
	I	1×10^{-3} (4×10^{-5})	
	Plutonium-242 S	6×10^{-8} (2×10^{-9})	
	I	1×10^{-6} (4×10^{-8})	
	Plutonium-243 S	6×10^{-2} (2×10^{-3})	
	I	8×10^{-2} (3×10^{-3})	
	Plutonium-244 S	6×10^{-8} (2×10^{-9})	
	I	1×10^{-6} (4×10^{-8})	

TABLE 7-1 (Continued)

Agency	Description		Value	References
NRC	Maximum concentration above background in restricted areas of:		pCi/ml (Bq/ml)	NRC 1988[a] 10 CFR 20.103(a)
	Plutonium-238	S	$2x10^{-6}$ ($7x10^{-8}$)	
		I	$3x10^{-5}$ ($1x10^{-6}$)	
	Plutonium-239	S	$2x10^{-6}$ ($7x10^{-8}$)	
		I	$4x10^{-5}$ ($1x10^{-6}$)	
	Plutonium-240	S	$2x10^{-6}$ ($7x10^{-8}$)	
		I	$4x10^{-5}$ ($1x10^{-6}$)	
	Plutonium-241	S	$9x10^{-5}$ ($3x10^{-6}$)	
		I	$4x10^{2}$ ($1x10^{1}$)	
	Plutonium-242	S	$2x10^{-6}$ ($7x10^{-8}$)	
		I	$4x10^{-5}$ ($1x10^{-6}$)	
	Plutonium-243	S	2 ($7x10^{-2}$)	
		I	2 ($7x10^{-2}$)	
	Plutonium-244	S	$2x10^{-6}$ ($7x10^{-8}$)	
		I	$3x10^{-5}$ ($1x10^{-6}$)	
b. Water:				
EPA ODW	MCL		pCi/L (Bq/L)	EPA 1988a 40 CFR 141.15
	Gross alpha particle activity (excluding radon and uranium)		15 ($6x10^{-1}$)	
NRC	Maximum concentration above background released at the boundary of power plant:		pCi/ml (Bq/ml)	NRC 1988[a] 10 CFR 20.106(a)
	Plutonium-238	S	5 (0.2)	
		I	30 (1.1)	
	Plutonium-239	S	5 (0.2)	
		I	30 (1.1)	
	Plutonium-240	S	5 (0.2)	
		I	30 (1.1)	
	Plutonium-241	S	2x102 (7.4)	
		I	$1x10^{3}$ (37.0)	
	Plutonium-242	S	5 (0.2)	
		I	30 (1.1)	
	Plutonium-243	S	$3x10^{2}$ (11.1)	
		I	$3x10^{2}$ (11.1)	
	Plutonium-244	S	4 (0.1)	
		I	10 (0.4)	

TABLE 7-1 (Continued)

Agency	Description	Value	References
c. Nonspecific media:			
EPA	Reportable quantity	Ci (Bq)	EPA 1989
	Plutonium-234	1000 ($3.7x10^{13}$)	
	Plutonium-235	1000 ($3.7x10^{13}$)	
	Plutonium-236	0.1 ($3.7x10^{9}$)	
	Plutonium-237	1000 ($3.7x10^{13}$)	
	Plutonium-238	0.01 ($3.7x10^{8}$)	
	Plutonium-239	0.01 ($3.7x10^{8}$)	
	Plutonium-240	0.01 ($3.7x10^{8}$)	
	Plutonium-241	1 ($3.7x10^{8}$)	
	Plutonium-242	0.01 ($3.7x10^{8}$)	
	Plutonium-243	1000 ($3.7x10^{13}$)	
	Plutonium-244	0.01 ($3.7x10^{8}$)	
	Plutonium-245	100 ($3.7x10^{12}$)	
Guidelines:			
EPA	Occupational - the committed effective dose equivalent (internal) and annual effective dose equivalent (external) combined	5 rem/yr (50 mSv)	EPA 1987
FRC	Individual - whole body exposure	0.5 rem/yr (5 mSv)	FRC 1960[b]
FRC	Individual - operational guide for "suitable sample of population" when individual whole body doses are not known	0.17 rem/yr (1.7 mSv)	FRC 1960[b]
EPA	Occupational ALI for inhalation of class W forms of[c]:	pCi (Bq)	EPA 1988b
	Plutonium-234	$2x10^{8}$ ($8x10^{6}$)	
	Plutonium-235	$3x10^{12}$ ($1x10^{11}$)	
	Plutonium-236	$2x10^{4}$ ($7x10^{2}$)	
	Plutonium-237	$3x10^{9}$ ($1x10^{8}$)	
	Plutonium-238	$7x10^{3}$ ($3x10^{2}$)	
	Plutonium-239	$6x10^{3}$ ($2x10^{2}$)	
	Plutonium-240	$6x10^{3}$ ($2x10^{2}$)	
	Plutonium-241	$3x10^{5}$ ($1x10^{4}$)	

TABLE 7-1 (Continued)

Agency	Description	Value	References
	Plutonium-242	$7x10^3$ ($2x10^2$)	
	Plutonium-243	$4x10^{10}$ ($1x10^9$)	
	Plutonium-244	$7x10^3$ ($3x10^2$)	
	Plutonium-245	$5x10^9$ ($2x10^8$)	
	Plutonium-246	$3x10^8$ ($9x10^6$)	
EPA	Occupational ALI for inhalation of class Y forms of[c]:	pCi (Bq)	EPA 1988b
	Plutonium-234	$2x10^8$ ($7x10^6$)	
	Plutonium-235	$3x10^{12}$ ($9x10^{10}$)	
	Plutonium-236	$4x10^4$ ($2x10^3$)	
	Plutonium-237	$3x10^9$ ($1x10^8$)	
	Plutonium-238	$2x10^4$ ($7x10^2$)	
	Plutonium-239	$2x10^4$ ($6x10^2$)	
	Plutonium-240	$2x10^4$ ($6x10^2$)	
	Plutonium-241	$8x10^5$ ($3x10^4$)	
	Plutonium-242	$2x10^4$ ($6x10^2$)	
	Plutonium-243	$4x10^{10}$ ($1x10^9$)	
	Plutonium-244	$2x10^4$ ($7x10^2$)	
	Plutonium-245	$4x10^9$ ($2x10^8$)	
	Plutonium-246	$3x10^8$ ($1x10^7$)	
EPA	Occupational ALI for ingestion of[d]:	pCi (Bq)	EPA 1988b
	Plutonium-234	$8x10^9$ ($3x10^8$)	
	Plutonium-235	$9x10^{11}$ ($3x10^{10}$)	
	Plutonium-236	$2x10^6$ ($9x10^4$)	
	Plutonium-237	$1x10^{10}$ ($5x10^8$)	
	Plutonium-238	$9x10^5$ ($3x10^4$)	
	Plutonium-239	$8x10^5$ ($3x10^4$)	
	Plutonium-240	$8x10^5$ ($3x10^4$)	
	Plutonium-241	$4x10^7$ ($1x10^6$)	
	Plutonium-242	$8x10^5$ ($3x10^4$)	
	Plutonium-243	$2x10^{10}$ ($6x10^8$)	
	Plutonium-244	$8x10^5$ ($3x10^4$)	
	Plutonium-245	$2x10^9$ ($8x10^7$)	
	Plutonium-246	$4x10^8$ ($1x10^7$)	
EPA	Occupational DAC for inhalation of class W forms of[e]:	pCi/cm^3 (Bq/m^3)	EPA 1988b
	Plutonium-234	$9x10^{-2}$ ($3x10^3$)	
	Plutonium-235	$1x10^3$ ($5x10^7$)	
	Plutonium-236	$8x10^{-6}$ ($3x10^{-1}$)	
	Plutonium-237	1 ($5x10^4$)	
	Plutonium-238	$3x10^{-6}$ ($1x10^{-1}$)	
	Plutonium-239	$3x10^{-6}$ ($1x10^{-1}$)	

TABLE 7-1 (Continued)

Agency	Description	Value	References
	Plutonium-240	$3x10^{-6}$ ($1x10^{-1}$)	
	Plutonium-241	$1x10^{-4}$ (5)	
	Plutonium-242	$3x10^{-6}$ ($1x10^{-1}$)	
	Plutonium-243	$2x10^{1}$ ($6x10^{5}$)	
	Plutonium-244	$3x10^{-6}$ ($1x10^{-1}$)	
	Plutonium-245	2 ($7x10^{4}$)	
	Plutonium-246	$1x10^{-1}$ ($4x10^{3}$)	
EPA	Occupational DAC for inhalation of class Y forms of[e]:	pCi/cm^3 (Bq/m^3)	EPA 1988b
	Plutonium-234	$8x10^{-2}$ ($3x10^{3}$)	
	Plutonium-235	$1x10^{3}$ ($4x10^{7}$)	
	Plutonium-236	$2x10^{-5}$ ($7x10^{-1}$)	
	Plutonium-237	1 ($5x10^{4}$)	
	Plutonium-238	$8x10^{-6}$ ($3x10^{-1}$)	
	Plutonium-239	$7x10^{-6}$ ($3x10^{-1}$)	
	Plutonium-240	$7x10^{-6}$ ($3x10^{-1}$)	
	Plutonium-241	$3x10^{-4}$ ($1x10^{1}$)	
	Plutonium-242	$7x10^{-6}$ ($3x10^{-1}$)	
	Plutonium-243	$2x10^{1}$ ($6x10^{5}$)	
	Plutonium-244	$7x10^{-6}$ ($3x10^{-1}$)	
	Plutonium-245	2 ($6x10^{4}$)	
	Plutonium-246	$1x10^{-1}$ ($4x10^{3}$)	

*See Glossary and Appendix B for definitions of units.

ALI = Annual Limit of Intake
DAC = Derived Air Concentration
EPA = Environmental Protection Agency
FRC = Federal Radiation Council
I = Insoluble
ICRP = International Commission for Radiation Protection
MCL = Maximum Contaminant Level
mSv = millisievert
NRC = Nuclear Regulatory Commission
OCW = Office of Drinking Water
S = Soluble

TABLE 7-1 (Continued)

Agency	Description	Value	References

[a]The Nuclear Regulatory Commission limits in 10 CFR 20 are in the process of revision.
[b]FRC guidance for occupational exposure is superseded by EPA (1987) Federal Radiation Protection Guidance.
[c]Conversion of the ALI for occupational settings to apply to exposure of persons in the general population is:

$$ALI_i = ALI * 0.1$$

where ALI_i is the intake for the general population, ALI is the intake for occupational exposures and 0.01 is the ratio of the dose limit to the individual (0.5 rem/yr) and the dose limit for occupational workers (5 rem/yr).
[d]Based on a fractional uptake from the small intestine to blood (f_1) of 0.001.
[e]Conversion of the DAC for occupational exposure to apply to the general public is:

$$DAC_i = DAC * 0.03$$

where DAC_i refers to the "Derived Air Concentration" for exposure to the general population and 0.03 represents the adjustment for hours of exposure (168 hrs per month occupational vs. 720 hr per month of continuous exposure), breathing rate (29 m^3/day for occupational vs. 22 m^3/day for the general population) and dose limits (0.5 rem/yr for individuals vs. 5 rem/yr for occupational settings).

8. REFERENCES

*Acquavella J, Wilkinson G, Tietjen G, et al. 1983a. A melanoma case-control study at the Los Alamos National Laboratory. Health Phys 45:587-592.

Acquavella J, Wilkinson G, Wiggs L, et al. 1983b. An evaluation of cancer incidence among employees at the Los Alamos National Laboratory. LA-UR-83-62. Los Alamos, NM: Los Alamos National Laboratory.

*Adriano D, Corey 3, Dahlman R. 1980. Plutonium contents of field crops in the southeastern United States. In: Hanson W, ed. Transuranic elements in the environment. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DOE/TIC-22800.

*Aghamohammadi S, Goodhead D, Savage J. 1988. Induction of sister chromatid exchanges (SEC) in GO lymphocytes by plutonium-238 alpha-particles. Int J Radiat Biol 53:909-915.

Anderson E, Holland L, Prine J, et al. 1974. Lung irradiation with static plutonium microspheres. In: Karbe E, Park J, eds. Experimental lung cancer. Carcinogenesis and bioassays. New York: Springer-Verlag, 430-442.

Anderson E, Holland L, Prine J, et al. 1977. Lung response to localized irradiation from plutonium microspheres. In: Walton W, ed. Inhaled Particles. Vol 4. New York: Pergamon Press, 615-623.

*Anderson E, Holland L, Prine J, et al. 1979. Tumorigenic hazard of particulate alpha activity in Syrian hamster lungs. Radiat Res 78:82-97.

*Andreozzi U, Clemente G, Ingrao G, et al. 1983. Long-term 238Pu and 239Pu retention and organ distribution in mice at low doses. Health Phys 44:505-511.

Andreozzi U, Addis L, Quaggia S. 1985. Metabolic behaviour of plutonium in mice. In: Priest N, ed. Metals in bone. Lancaster, England: MTP Press, Ltd., 243-245.

*Aoyagi H, Yoshida Z, Kihara S. 1987. Plutonium and uranium ion determination and differentiation based on twin electrode flow coulometry. Anal Chem 59:400-405.

*Cited in text.

8. REFERENCES

*APHA. 1977. American Public Health Association. In: Katz M, ed. Methods of air sampling and analysis. 2nd ed. APHA Intersociety Committee, 642-646.

*Ash P, Parker T. 1978. The ultrastructure of mouse testicular interstitial tissue containing plutonium-239 and its significance in explaining the observed distribution of plutonium in the testis. Int J Radiat Biol 34:523-536.

*ASTM. 1981. Standard test method for alpha particle radioactivity of water. ASTM standards, designation D-1943-81. American Society for Testing and Materials, Philadelphia, PA, l-5.

*ASTM. 1982a. Standard practice for alpha spectrometry of water. ASTM standards designation D-3084-75. American Society for Testing and Materials, Philadelphia, PA, l-5.

*ASTM. 1982b. Standard test method for isotopic uranium in water by radiochemistry. ASTM standards designation D-3972-82. American Society for Testing and Materials, Philadelphia, PA, l-6.

*ASTM. 1987. Standard practices for the measurement of radioactivity. Annual book ASTM standards, designation D-3648-78. American Society for Testing and Materials, Philadelphia, PA, 1, 13-17.

Atherton D, Stevens W, Bates D, et al. 1976. Skeletal retention of 239Pu(IV) in beagles injected at three months of age. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 71-80.

*ATSDR. 1990. Toxicological profile for radon. U.S. Department of Health and Human Services. Public Health Service, Agency for Toxic Substances and Disease Registry, Atlanta, GA.

Bair W. 1970. Toxicology of inhaled plutonium - experimental animal studies. Presented at seminar on radiation protection problems relating to transuranium elements, Karlsruhe, Germany.

*Bair W. 1985. ICRP work in progress: Task Group to review models of the respiratory tract. Radio1 Prot Bull 63:5-6.

*Bair W, McClanahan B. 1961. Plutonium inhalation studies. II. Excretion and translocation of inhaled Pu-23902 dust. Arch Environ Health 2:48-55.

*Bair W, Thompson R. 1974. Plutonium: biomedical research. Science 183:715-722.

8. REFERENCES

*Bair W, Willard D. 1962. Plutonium inhalation studies. IV. Mortality in dogs after inhalation of Pu23902. Radiat Res 16:811-821.

*Bair W, Wiggins A, Temple L. 1962a. The effect of inhaled Pu23902 on the lifespan of mice. Health Phys 8:659-663.

*Bair W, Willard D, Herring J, et al. 1962b. Retention, translocation and excretion of inhaled Pu23902. Health Phys 8:639-649.

*Bair W, Park J, Clarke W. 1966. Long-term study of inhaled plutonium in dogs. AFWL-TR-65-214. Air Force Weapons Laboratory, Kirtland Air Force Base, New Mexico.

*Bair W, Ballou J, Park J, et al. 1973. Plutonium in soft tissues with emphasis on the respiratory tract. In: Hodge H, et al., eds. Uranium, plutonium - transplutonic elements. New York: Springer-Verlag, 503-568.

*Bair W, Willard D, Nelson I, et al. 1974. Comparative distribution and excretion of 237Pu and 239Pu nitrates in beagle dogs. Health Phys 27:392-396.

Bair W, Metivier H, Park J, et al. 1980. Comparison of early mortality in baboons and dogs after inhalation of 239PuO2. Radiat Res 82:588-610.

Ballou J, Hess J. 1972. Biliary plutonium excretion in the rat. Health Phys 22:369-372.

Ballou J, Oakley W. 1957. Absorption and decontamination of plutonium on rats. Biology Research Annual Report 1956 to U.S. Department of Energy, Washington, DC, by Hanford Atomic Products Operation, Richland, WA. Report NW-47500.

*Ballou J, George L II, Thompson R. 1962. The combined toxic effects of plutonium plus x-ray in rats. Health Phys 8:581-587.

*Ballou J, Thompson R, Clarke W, et al. 1967. Comparative toxicity of plutonium-238 and plutonium-239 in the rat. Health Phys 13:1087-1092.

*Ballou J, Park J, Morrow W. 1972. On the metabolic equivalence of ingested, injected and inhaled 239Pu citrate. Health Phys 22:857-862.

Barnhart B, Cox S. 1979. Mutagenicity and cytotoxicity of 4.4-mev alpha particles emitted by plutonium-238. Radiat Res 80:542-548.

*Baxter D, Rosenthal M, Russell J, et al. 1973. Comparison of monomeric and polymeric plutonium in the dog and mouse. Radiat Res 54:556-565.

8. REFERENCES

*Beechey C, Green D, Humphreys E, et al. 1975. Cytogenetic effects of plutonium-239 in male mice. Nature 256:577-578.

*BEIR IV. 1988. Health risks of radon and other internally deposited alpha-emitters. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

*Bell J, Bates T. 1988. Distribution coefficients of radionuclides between soils and groundwaters and their dependence on various test parameters. Sci Total Environ 69:297-317.

*Benjamin S, Brooks A, McClellan R. 1976. Biological effectiveness of 239Pu, 144Ce and 90Sr citrate in producing chromosome damage, bone-related tumours, liver tumours and life shortening in the Chinese hamster. In: Biological and Environmental Effects of Low-Level Radiation. Vienna: International Atomic Energy Agency, 143-152.

*Bennett B. 1976a. Transfer of plutonium from the environment to man. In: Proceedings of the international symposium on the management of wastes from the LWR fuel cycle. CONF-76-0701.

*Bennett B. 1976b. Transuranic element pathways to man. IAEA-SM-199/40. In: Transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 367-383.

Beno M. 1968. A study of "haemosiderin" in the marrow of the femur of normal young adult rabbits compared with that in rabbits 4 months after an intravenous injection of 239Pu(N03)4. Br J Haematol 15:487-493.

Bensted J, Taylor D, Sowby F. 1965. The carcinogenic effects of americium 241 and plutonium 239 in the rat. Br J Radiol 38:920-925.

*Bernhardt D. 1976. Evaluation of sample collection and analysis techniques for environmental plutonium. In: Selected topics: Transuranium elements in the general environment. 1978. Environmental Protection Agency, Office of Radiation Programs. Washington, D.C.

Bhattacharyya M, Lindenbaum A. 1976a. Association of plutonium with isolated liver parenchymal cells following injection of monomeric plutonium into mice. Radiat Res 66:552-565.

Bhattacharyya M, Lindenbaum A. 1976b. Monomeric plutonium and mouse liver parenchymal cells: deposition and DTPA-induced removal. In: Webster S, ed. The Health Effects of Plutonium and radium. Salt Lake City, UT: J W Press, 233-243.

8. REFERENCES

Bhattacharyya M, Larsen R, Oldham R, et al. 1986. Effects of duration of fast and animal age on the gastrointestinal absorption of plutonium. Radiat Res 107:73-82.

*Bite E, Harris D, Schnizlein C, et al. 1979. Methods to evaluate the effects of toxic materials deposited in the lung on immunity in lung-associated lymph nodes. Drug Chem Toxicol 2:35-47.

Bleaney B, Vaughan J. 1971. Distribution of 239Pu in the bone marrow and on the endosteal surface of the femur of adult rabbits following injection of 239Pu(N03),. Br J Radio1 44:67-73.

*Bogen D, Krey P, Volchok H, et al. 1988. Threat to the New York City water supply - plutonium. Sci Total Environ 70:101-118.

*Bomford J, Harrison J. 1986. The absorption of ingested Pu and Am in newborn guinea pigs. Health Phys 51:804-808.

*Bondietti E, Reynolds S, Shanks M. 1976. Interaction of plutonium with complexing substances in soils and natural waters. IAEA-SM-199/51. In: Transuranium nuclides in the environment. Proceedings of the symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 273-287.

*Brandom W. 1985. Somatic cell chromosome changes in a population exposed to low levels of ionizing radiation. Washington, DC: U.S. Department of Energy. NTIS no. DOE/EV/03639-Tl.

*Brandom W, Archer P, Bloom A, et al. 1979. Chromosome changes in somatic cells of workers with internal depositions of plutonium. In: Biological implications of radionuclides released from nuclear industries. Vol 2. STI/PUB/522. Vienna: International Atomic Energy Agency, 195-210.

*Brooks A. 1975. Chromosome damage in liver cells from low dose rate alpha, beta, and gamma irradiation: Derivation of RBE. Science 190:1090-1092.

*Brooks A, LaBauve R, McClellan R, et al. 1976a. Chromosome aberration frequency in blood lymphocytes of animals with 239Pu lung burdens. In: Radiation and the lymphatic system. National Technical Information Service. Springfield, VA. NTIS no. CONF-740930.

*Brooks A, McClellan R, Peters R, et al. 1976b. Effect of size and alpha flux of 239PuO2 particles on production of chromosome aberrations in liver of Chinese hamster. In: Biological and environmental effects of low-level radiation. Vol 2. Vienna: International Atomic Energy Agency, 131-142.

8. REFERENCES

*Brooks A, Die1 J, McClennan R. 1979. The influence of testicular microanatomy on the potential genetic dose from internally deposited 239Pu citrate in Chinese hamster, mouse, and man. Radiat Res 77:292-302.

*Brooks A, Benjamin S, Hahn F, et al. 1983. The induction of liver tumors by plutonium-239 citrate or plutonium-239 dioxide particles in the Chinese hamster. Radiat Res 96:135-151.

Brooks A, Guilmette R, Hahn F, et al. 1985. Uptake and clearance of plutonium-238 from intact liver and liver cells transplanted into fat pads of F344/N rats. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-114.

Brooks A, Guilmette R, Hahn F, et al. 1986. Uptake and clearance of plutonium-238 from liver cells transplanted into fat pads of F344 rats. Int J Radiat Biol Relat Stud Phys Chem Med 50:631-640.

*Brouns R. 1980. Analysis. In: Wock 0, ed. Plutonium handbook: A guide to the technology. Vol II. The American Nuclear Society, Illinois, 709-720, 921-933.

*Bruenger F, Stevens W, Atherton D, et al. 1978. Distribution of 239Pu in neonatal beagles. In: Mahlum D, et al., eds. Developmental toxicology of energy-related pollutants. Proceedings 17th Hanford Biology Symposium, Richland, WA. Springfield, VA: Technical Information Center, U.S. Department of Energy, 344-360.

*Bruenger F, Stevens W. Stover B, et al. 1980. The distribution and pathological effects of Pu in juvenile beagles. Radiat Res 84:325-342.

Bruenger F, Smith J, Atherton D, et al. 1983. Skeletal retention and distribution of 226Ra and 239 Pu in beagles injected at ages ranging from 2 days to 5 years. Health Phys 44 Suppl:513-527.

*Buldakov L, Lyubchanskii E, Moskalev Y, et al. 1970. Problems of plutonium toxicology. Atom Publications, Moscow, 1969. LF-tr-41, UC-48. (Translation and production prepared for U.S. Atomic ,Energy Commission.)

*Buldakov L, Kalmykova Z, Nifatov A, et al. 1972. Metabolism and biological effects of inhaled 241Am and 239Pu in dogs. Health Phys 22:873-874.

*Bunzl K, Kracke W. 1987. Simultaneous determination of plutonium and americium in biological and environmental samples. J Radioanal Nucl Chem 115:13-21.

8. REFERENCES

*Carritt J, Fryxell R, Kleinschmidt J, et al. 1947. The distribution and excretion of plutonium administered intravenously to the rat. J Biol Chem 171:273-283.

*Cataldo D, Wildung R, Garland T. 1987. Speciation of trace inorganic contaminants in plants and bioavailability to animals: An overview. J Environ Qua1 16:289-295.

*Chen D, Strniste G, Tokita N. 1984. The genotoxicity of alpha particles in human embryonic skin fibroblasts. Radiat Res 100:321-327.

*Choppin G, Morse J. 1987. Laboratory studies of actinides in marine systems. In: Pinder J, et al., eds. Environmental research on actinide elements. Office of Science and Technical Information. U.S. Department of Energy, Springfield, VA. NTIS no. CONF-841142.

*Choppin G, Rydberg J. 1980. Nuclear chemistry: Theory and applications. New York: Pergammon Press, 242-264, 488-559.

Clarke W, Bair W. 1964. Plutonium inhalation studies--VI. Pathologic effects of inhaled plutonium particles in dogs. Health Phys 10:391-398.

Clarke W, Park J, Palotay J, et al. 1966. Plutonium inhalation studies--VII. Bronchiole-alveolar carcinomas of the canine lung following plutonium particle inhalation. Health Phys 12:609-613.

*Cleveland J. 1970. The chemistry of plutonium. New York: Gordon and Breach, 3-8, 291-322.

*Cleveland J, Rees T. 1982. Characterization of plutonium in groundwater near the Idaho chemical processing plant. Environ Sci Technol 16:437-439.

*Cobb J, Eversole B, Archer P, et al. 1982. Plutonium burdens in people living around the Rocky Flats plant. Report to U.S. Environmental Protection Agency, Environmental Monitoring and Support Laboratory, Las Vegas, NV. NTIS no. PB83-137372.

*Cochran T, Jee W, Stover B, et al. '1962. Liver injury in beagles with Pu239: Distribution, dosage and damage. Health Phys 8:699-703.

*Corey J, Boni A. 1976. Removal of plutonium from drinking water by community water treatment facilities. IAEA-SM-199/81. In: Transuranium nuclides in the environment. Proceedings of the symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 401-408.

8. REFERENCES

*Corey J, Finder J III, Watts J, et al. 1982. Stack-released plutonium in the terrestrial environment of a chemical separations facility. Nut 1 Saf 23:310-319.

Craig D, Mahlum D, Klepper E. 1974. The relative quantity of airborne plutonium deposited in the respiratory tract and on the skin of rats. BNWL-SA-4867. Battelle Pacific Northwest Laboratory, Richland, WA. NTIS no. CONF-740702-1.

*Cristy M, Leggett R. 1986. Determination of metabolic data appropriate for HLW dosimetry. II. Gastrointestinal absorption. NUREG/CR-3572 Vol II. OP.NL/TM-8932/V2. Report to U.S. Department of Energy, Washington, DC, by Oak Ridge National Laboratory, Oak Ridge, TN.

*Crump K, Ng T, Cuddihy R. 1987. Cancer incidence patterns in the Denver metropolitan area in relation to the Rocky Flats Plant. Am J Epidemiol 126:127-135.

Dagle G, Sanders C, Park J, et al. 1980. Pulmonary carcinogenesis with inhaled plutonium in rats and dogs. In: Sanders C, et al., eds. Pulmonary toxicology of respirable particles. 19th Hanford Life Sciences Symposium, Richland, WA. U.S. Department of Energy, Washington, DC.

*Dagle G, Cannon W, Stevens D, et al. 1983. Comparative disposition of inhaled 238Pu and 239Pu nitrates in beagles. Health Phys 44:275-277.

*Dagle G, Bristline R, Lebel J, et al. 1984. Plutonium-induced wounds in beagles. Health Phys 47:73-84.

Dagle G, Park J, Weller R, et al. 1985. Skeletal lesions from inhaled plutonium in beagles. In: Priest N, ed. Metals in bone. Lancaster, England: MTP Press, Ltd., 333-341.

*Dagle G, Adee R, Apley G, et al. 1985. Inhaled plutonium nitrate in dogs. Annual Report to U.S. Department of Energy, Washington, DC, by Pacific Northwest Laboratory, Richland, WA. NTIS no. DE-85009365.

*Dagle G, Park J, Weller R, et al. 1986. Pathology associated with inhaled plutonium in beagles. In: Thompson *R, McHaffey J, ids.* Life-span radiation effects studies in animals: What can they tell us? Proceedings 22nd Hanford Life Sciences Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DE87000490.

*Dagle G, Adee R, Buschbom R, et al. 1988. Inhaled plutonium nitrate in dogs. Part 1. Biomedical sciences. 1987 Annual Report to U.S. Department of Energy, Office of Energy Research by Pacific Northwest Laboratory, Richland, WA. PNL-6500-Part 1. NTIS no. DE88-011885.

8. REFERENCES

*Daly G, Kluk A. 1975. Transuranium nuclides in the environment from management of solid radioactive waste. Environmental Quarterly, HASL-291. New York: Health and Safety Laboratory, Energy Research and Development Administration, I-110-126.

Danpure C, Raylor D. 1974. The effect of internally deposited plutonium-239 on the lysosomes of rat liver. Radiat Res 59:679-692.

*David A, Harrison J. 1984. The absorption of ingested neptunium, plutonium and americium in newborn hamsters. Int J Radiat Biol 46:279-286.

*Die1 J, Lundgren D. 1982. Repeated inhalation exposure of beagle dogs to 239PuO2: Retention and translocation. Health Phys 43:655-662.

Die1 J, Short R. 1979. Collagen localization in lung parenchyma irradiated by inhaled 238Pu0, particles. Radiat Res 79:417-423.

*Die1 J, Mewhinney J, Snipes M. 1981. Distribution of inhaled plutonium-238 dioxide particles in Syrian hamster lungs. Radiat Res 88:299-312.

Die1 J, Hahn F, Muggenburg B. 1985. Repeated inhalation exposure of beagle dogs to aerosols of 239PuO2. IX. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-114.

Die1 J, Hahn F, Muggenburg B. 1987. Repeated inhalation exposure of beagle dogs to aerosols of 239PuO2. XI. Annual Report to U.S.

Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-120.

*DOT. 1988. Department of Transportation, Research and Special Programs Administration. Code of Federal Regulations. 49 CFR 170.

Dougherty J, Rosenblatt L. 1970. The comparative toxicity of 226Ra, 239Pu, 228Th, 228Ra, and 90Sr to leukocytes of beagles. Radiat Res 43:56-70.

*Dougherty J, Rosenblatt L. 1971. Long-term hematological effects of internal emitters in beagles. Radiat Res 48:319-331.

Dougherty T, Stover B, Dougherty J, et al. 1962. Studies of the biological effects of Ra-226, Pu-239, Ra-228(MsThi), Th-228(RdTh), and Sr-90 in adult beagles. Radiat Res 17:625-681.

*Durbin P, Jeung N, Schmidt C. 1985. Plutonium-238(IV) in monkeys: Overview of metabolism. NUREGICR-4355. LBL-20022. Vol 1. Lawrence Berkeley Laboratory, University of California, Berkeley, CA.

8. REFERENCES

*Edelson M, DeKalb E, Winge R, et al. 1986. Analytical atomic spectroscopy of plutonium--I. High resolution spectra of plutonium emitted in an inductively coupled plasma. Spectrochim Acta 41B:475-486.

*Edgington D, Alberts J, Wahlgren M, et al. 1976. Plutontilm and americium in Lake Michigan sediments. IAEA-SM-199/47. In: Transuranium nuclides in the environment. Proceedings of the symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 493-514.

*Eisenbud M. 1987. Environmental radioactivity from natural, industrial, and military sources. 3rd ed. New York: Academic Press, Inc., 366, 376, 422-423.

*Emery R, Klopfer D, McShane M. 1980. The migration of plutonium from a freshwater ecosystem at Hanford. In: Hanson W, ed. Transuranic elements in the environment. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DOELTIC-22800.

EPA. 1976. Availability, uptake and translocation of plutonium within biological systems: A review of significant literature. EPA/600-3-76-043.

*EPA. 1977. Proposed guidance on dose limits for persons exposed to transuranium elements in the general environment. EPA 520/4-77-016. Office of Radiation Programs, Washington, DC.

*EPA. 1980. Prescribed procedures for measurement of radioactivity in drinking water. EPA 600/4-80-032. Cincinnati, OH: Environmental Monitoring and Support Laboratory.

*EPA. 1984. Radiochemistry procedures manual. EPA/520/5-84-006. Cincinnati, OH: Eastern Environmental Radiation Facility.

*EPA. 1987. Radiation protection guidance to federal agencies for occupational exposure; approval of Environmental Protection Agency recommendations. Federal Register 52:2823-2834.

*EPA. 1988a. Environmental Protection Agency. Code of Federal Regulations. 40 CFR 141.

*EPA. 1988b. Limiting values of radionuclide intake and air concentration and dose conversion factors for inhalation, submersion, and ingestion. Federal Guidance Report No. 11. Washington, DC: U.S. Environmental Protection Agency, Office of Radiation Programs. EPA-520/l-88-020.

*EPA. 1989. Reportable quantity adjustment--radionuclides; final rules. Fed Reg 54:22524-22543.

8. REFERENCES

Fabrikant J, Hsu T, Knudson D, et al. 1973. Effect of LET on radiation carcinogenesis: comparison of 239Pu, 241Am, 32P, and X-rays on the production of osteosarcomas in rats. In: Sanders C, et al., eds. Radionuclide carcinogenesis. Symposium Series 29. Washington, D.C.: U.S. Atomic Energy Commission, 322-346.

*Facer G. 1980. Quantities of transuranic elements in the environment from operations relating to nuclear weapons. In: Hanson W, ed. Transuranic elements in the environments. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DOE/TIC-22800.

Filipy R, Bair W, Buschbom R. 1985. Cigarette smoke and plutonium. Part I: Biomedical sciences. 1984 Annual report to U.S. Department of Energy, Washington, DC, by Pacific Northwest Laboratory, Richland, WA. PNL-5500.

*Frazier M, Sneed T, Scott L, et al. 1988. Radiation-induced carcinogenesis in dogs. PNL-SA-14723. Annual Report to U.S. Department of Energy, Washington, DC, by Pacific Northwest Laboratory, Richland, WA.

*FRc . 1960. Radiation protection guidance for federal agencies. Federal Radiation Council. Federal Register 60:4402-4403.

*Fritsch P, Beauvallet M, Masse R, et al. 1980. Short-term assays for risk evaluation of alpha irradiation. In: Sanders C, et al., eds. Pulmonary toxicology of respirable particles. 19th Hanford Life Sciences Symposium, Richland, WA. U.S. Department of Energy, Washington, DC.

*Fritsch P, Beauvallet M, Moutairou K, et al. 1987. Acute lesions induced by alpha-irradiation of intestine after plutonium gavage of neonatal rats. Int J Radiat Biol Relat Stud Phys Chem Med 52:1-6.

*Fritsch P, Mautairou K, Lataillade G, et al. 1988. Localization of plutonium retention in the small-intestine of the neonatal rat, guinea-pig, baboon and maraca after Pu-citrate ingestion. Int J Radiat Biol 54:537-543.

*Garland T, Cataldo D, Wildung R. 1981. Absorption, transport, and chemical fate of plutonium in soybean plants. J Agric Food Chem 29:915-920.

*Garland T, Cataldo D, McFadden K, et al. 1987. Factors affecting absorption, transport, and form of plutonium in plants. In: Pinder J, et al., eds. Environmental research on actinide elements. Office of Science and Technical Information. U.S. Department of Energy, Springfield, VA. NTIS no. CONF-841142.

8. REFERENCES

Gearhart J, Die1 J, McClellan R. 198@. Intrahepatic distribution of plutonium in beagles. Radiat Res 841343-352.

*Generoso W, Cain K, Cacheiro N, et al. 1985. 239-Plutonium-ind,Jced heritable translocations in male mice. Mutat Res 152:49-52.

Gilbert E. 1980. Mortality of Hanford radiation workers. In: Rom W, Archer V, eds. Health implications of new energy technologies. Ann Arbor, MI: Ann Arbor Science, 119-127.

*Gilbert E, Marks S. 1979. An analysis of the mortality of workers in a nuclear facility. Radiat Res 79:122-148.

*Gillett N, Muggenburg B, Mewhinney J, et al. 1988. Primary liver tumors in beagle dogs exposed by inhalation to aerosols of plutonium-238 dioxide. Am J Path01 133:265-276.

*Gonzalez D. 1988. On-site environmental report for the Nevada test site (January 1987 through December 1987). Draft. Contract DE-AC08-84NV10327. Environmental Surveillance Group, Laboratory Operations Section, Environmental Sciences Department, Reynolds Electrical and Engineering Co., Inc., Las Vegas, NV.

*Grahn D, Lee C, Farrington B. 1983. Interpretation of cytogenetic damage induced in the germ line of male mice exposed for over 1 year to 239Pu alpha particles, fission neutrons, or 60C0 gamma rays. Radiat Res 95:566-583.

Green D, Howells G, Humphreys E. 1975. Distribution of 239Pu in male CBA mice after intravenous and intraperitoneal injection. Health Phys 29:798-799.

Green D, Howells G, Humphreys E, et al. 1975. Localization of plutonium in mouse testes. Nature 255:77.

*Green D, Howells G, Humphreys E, et al. 1976. Radiation dose to mouse testes from 239Pu. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 21-31.

*Green D, Howells G, Vennart J, et al. 1977. The distribution of plutonium in the mouse ovary. Int J Appl Radiat Isot 28:497-502.

Green D, Howells G, Thorne M. 1978. Plutonium-239 deposition in the skeleton of the mouse. Int J Radiat Biol 34:27-36.

*Green D, Howells G, Watts R. 1979. Plutonium in the tissues of foetal, neonatal and suckling mice after Pu-administration to their dams. Int J Radiat Biol 35:417-432.

8. REFERENCES

Grube B, Stevens W, Atherton D, et al. 1976. Cellular and extracellular retention and distribution of plutonium in rat liver. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 183-198.

Grube B, Stevens W, Atherton D. 1978. The retention of plutonium in hepatocytes and sinusoidal lining cells isolated from rat liver. Radiat Res 73:168-179.

*Guilmette R, Lindenbaum A, Friedman A, et al. 1978. Influence of injected mass of plutonium on its biological distribution. Health Phys 35:529-536.

*Guilmette R, Die1 J, Muggenburg B, et al. 1984. Biokinetics of inhaled plutonium-239 dioxide in the beagle dog: Effect of aerosol particle size. Int J Radiat Biol Relat Stud Phys Chem Med 45:563-581.

Guilmette R, Muggenburg B, Boecker B. 1985. Biokinetics of 239PuO2 inhaled by aged dogs. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. I&F-114.

*Guilmette R, Muggenburg B, Die1 J. 1986. Biokinetics of 239Pu in immature dogs that inhaled 239PuO2. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-115.

*Guilmette R, Muggenburg B, Hahn F, et al. 1987. Toxicity of 234PuO2 in immature beagle dogs. IX. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. IMF-120.

*Hahn F, Mewhinney J, Merickel B, et al. 1981. Primary bone neoplasms in beagle dogs exposed by inhalation to aerosols of plutonium-238 dioxide. J Nat1 Cancer Inst 67:917-928.

*Hahn F, Brooks A, Mewhinney J. 1984. A pulmonary sarcoma in a Rhesus monkey after inhalation of plutonium dioxide. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-113.

*Hakonson T, Nyhan J. 1980.. Ecological relationships of plutonium in southwest ecosystems. In: Hanson W, ed. Transuranic elements in the environment. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DOE/TIC-22800.

*Hammond S, Putzier E. 1964. Observed effects of plutonium in wounds over a long period of time. Health Phys 10:399-406.

8. REFERENCES

*Hamrick P, Walsh P. 1974. Environmental radiation and the lung. Environ Health Perspect 9:33-52.

*Hanson W. 1975. Ecological considerations of the behavior of plutonium in the environment. Health Phys 28:529-537.

*Hardy E. 1973. Fallout program quarterly summary report. Health and Safety Laboratory. HASL-274. U.S. Atomic Energy Commission Report.

*Harley J. 1980. Plutonium in the environment--A review. J Radiat Res 21:83-104.

*Harrison J, David A. 1987. The effect of ingested mass on Pu absorption in the rat. Health Phys 53:187-189.

Harrison J, Stather J. 1982. The tissue distribution and excretion of actinides absorbed from the gastrointestinal tract of rodents. Health Phys 43:283-285.

*Harrison J, Cooper J, Bomford J, et al. 1986. The gastrointestinal absorption of organically bound forms of plutonium in fed and fasted hamsters. Int J Radiat Biol 50:1083-1091.

*Hayes D, LeRoy J, Cross F. 1976. Plutonium in Atlantic coastal estuaries in the Southeastern United States of America. IAEA-SM-199/84. In: Transuranium nuclides in the environment. Proceedings of the symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 79-87.

*Hempelmann L, Langham W, Richmond C, et al. 1973. Manhattan project plutonium workers: A twenty-seven year follow-up study of selected cases. Health Phys 25:461-479.

*Hetherington J, Jefferies D, Mitchell N, et al. 1976. Environmental and public health consequences of the controlled disposal of transuranic elements to the marine environment. IAEA-SM-199/11. In: Transuranium nuclides in the environment. Proceedings of the symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 139-153.

*Higgo J, Rees L. 1986. Adsorption of actinides by marine sediments: Effect of the sediment/seawater ratio on the measured distribution ratio. Environ Sci Technol 20:483-490.

*Hindman F. 1986. Actinide separations for alpha spectrometry using neodymium fluoride co-precipitation. Anal Chem 58:1238-1241.

*Hisamatsu S, Takizawa Y, Abe T. 1987. Ingestion intake of fallout Pu in Japan. Health Phys 52:193-200.

8. REFERENCES

Holland L, Prine J, Smith D, et al. 1976. Irradiation of the lung with static plutonium microemboli. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 127-138.

Humphreys E, Loutit J. 1980. Lesions in CBA mice from nanocurie amounts of 239Pu. Int J Radiat Biol 37:307-314.

Humphreys E, Metalli P, Seidel A, et al. 1976. The distribution of 239Pu in several strains of mice --A collaborative experiment. Int J Appl Radiat Isotop 27:507-513.

Humphreys E, Fisher G, Thorne M. 1977. The measurement of blood flow in mouse femur and its correlation with 239Pu deposition. Calcif Tiss Res 23:141-145.

*Humphreys E, Green D, Howells G, et al. 1982. Relationship between' blood flow, bone structure, and 239Pu deposition in the mouse skeleton, Calcif Tissue Int 34:416-421.

Humphreys E, Loutit J, Stones V. 1985. The induction, by 239Pu, of myeloid leukaemia and osteosarcoma in female CBA mice (interim results). In: Priest N, ed. Metals in bone. Lancaster, England: MTP Press, Ltd., 343-351.

*Humphreys E, Loutit J, Stones V. 1987. The induction by Pu-239 of myeloid-leukemia and osteosarcoma in female CBA mice. Int J Radiat Biol 51:331-339.

Hunt G, Leonard D, Lovett M. 1986. Transfer of environmental plutonium and americium across the human gut. Sci Total Environ 53:89-109.

*ICRP. 1972. The metabolism of compounds of plutonium and other actinides. ICRP Publication 19. International Commission on Radiological Protection. New York: Pergammon Press, 2-59.

*ICRP. 1975. Report of the Task Group on Reference Man. ICRP Publication 23. International Commission on Radiological Protection. New York: Pergammon Press, l-7.

*ICRP. 1977. Recommendations of the International Commission on Radiological Protection. ICRP Publication 26. New York: Pergammon Press, l-43.

*ICRP. 1978. Limits for intakes of radionuclides by workers. ICRP Publication 30. Part 1. International Commission on Radiological Protection. New York: Pergammon Press, 12-29.

8. REFERENCES

*ICRP. 1979. Limits for intakes of radionuclides by workers. ICRP Publication 30. International Commission on Radiological Protection. New York: Pergammon Press, 387-439.

*ICRP. 1982. Limits for intakes of radionuclides by workers. ICRP Publication 30. International Commission on Radiological Protection. New York: Pergammon Press, 105-107.

*ICRP. 1986. The metabolism of plutonium and related elements. ICRP Publication 48. International Commission on Radiological Protection. New York: Pergammon Press, l-98.

*International Atomic Energy Agency. 1982. Basic safety standards for radiation protection. Safety series No. 9. Vienna: International Atomic Energy Agency, 128-129.

*Iranzo E, Salvador S, Iranzo C. 1987. Air concentrations of 239Pu and 24OPu and potential radiation doses to persons living near Pu-contaminated areas in Palomares, Spain. Health Phys 52:453-461.

*James A. 1988. Lung dosimetry. In: Nazaroff W, Nero A, eds. Radon and its decay products in indoor air. New York: John Wiley 6 Sons, 259-309.

James A, Roy M. 1987. Dosimetry lung models. In: Gerber G, et al., eds. Age-related factors in radionuclide metabolism and dosimetry. Boston: Martinus Nijhoff Publishers, 95-108.

Jee W, Stover B, Taylor G, et al. 1962. The skeletal toxicity of Pu239 in adult beagles. Health Phys 8:599-607.

Jee W, Atherton D, Bruenger F, et al. 1976. Current status of Utah long-term 239Pu studies. In: Biological and environmental effects of low-level radiation. Vol 2. Vienna: International Atomic Energy Agency, 79-94.

Jee W, Dell R, Parks N, et al. 1985. Toxicity of plutonium and americium: Relationship of bone composition to location of 226Ra, 239Pu and 24&n-induced bone sarcomas. In: Priest N, ed. Metals in bone. Lancaster, England: MTP Press, Ltd., 155-174.

*Johnson C. 1981. Cancer incidence in an area contaminated with radionuclides near a nuclear installation. Ambio 10:176-182.

*Johnson C. 1988. Re: Mortality among plutonium and other radiation workers at a plutonium weapons facility. Am J Epidemiol 127:1321-1323.

8. REFERENCES

*Joshima H, Kashima M, Enomoto H, et al. 1981. Effect of polymeric plutonium on the hematopoietic activity in the bone marrow of mice. J Radiat Res 22:425-433.

Joshima H, Kashima M, Matsuoka 0. 1984. Diminished osmotic fragility of mouse erythrocytes following intravenous injection of polymeric plutonium. J Radiat Res 25:290-295.

*Kabata-Pendias A, Pendias H. 1984. Trace elements in soils and plants. Boca Raton, Florida: CRC Press, Inc., 147.

Kashima M, Mahlum D, Sikov M. 1972. Metabolism and effect of monomeric and polymeric plutonium in the immature rat liver. Health Phys 22:749-752.

*Kathren R, McInroy J, Swint M. 1987. Actinide distribution in the human skeleton. Health Phys 52:179-192.

*Kathren R, McInroy J, Reichert M, et al. 1988. Partitioning of 238Pu, 239Pu and 241Am in skeleton and liver of U.S. transuranium registry autopsy cases. Health Phys 54:181-188.

Katz J, Kornberg H, Parker H. 1953. Absorption of plutonium fed chronically to rats. I. Fraction deposited in skeleton and soft tissues following oral administration of solutions of very low mass concentration. Richland, WA: Hanford Atomic Products Operation. NTIS no. DE86015556.

*Katz J, Kornberg H, Parker H. 1955. Absorption of plutonium fed chronically to rats. I. Fraction deposited in skeleton and soft tissues following oral administration of solutions of very low mass concentration. Am J Roentgen01 73:303-308.

*Kawamura H. 1987. Plutonium and Am contamination of tourist property and estimated inhalation intake of visitors to Kiev after the Chernobyl accident. Health Phys 52:793-795.

Kawamura H, Tanaka G, McInroy J, et al. 1981. Concentration of 239, 24OPu in human autopsy tissues. Preliminary report of a comparative study on different populations. J Radiat Res 22:373-380.

*Kelman B, Sikov M, Hackett P. 1982a. Effects of monomeric 239Pu on the fetal rabbit. Health Phys 43:80-83.

Kelman B, Sikov M, Hackett P. 1982b. Effects of monomeric 239Pu on the pregnant rabbit. Health Phys 42:730-731.

8. REFERENCES

*Khodyreva M. 1966. Absorption of 239Pu through the skin of animals and its distribution in the organism. Distribution and biological effects of radioactive isotopes. AEC-TR-6944. U.S. Atomic Energy Commission.

*Kneale G, Mancuso T, Stewart A. 1981. Hanford radiation study III: A cohort study of the cancer risks from radiation to workers at Hanford (1944-77 deaths) by the method of regression models in life-tables. Br J Ind Med 38:156-166.

Kwadow M, Chevalier C. 1988. Occupational exposure to radionuclides in French nuclear power plants: Five years excretion monitoring results. Sci Total Environ 70:299-319.

*LaBauve R, Brooks A, Mauderly J, et al. 1980. Cytogenetic and other biological effects of 239PuO2 inhaled by the Rhesus monkey. Radiat Res 82:310-335.

*Lagerquist C, Hammond S, Bokowski D, et al. 1973. Distribution of plutonium and americium in occupationally exposed humans as found from autopsy samples. Health Phys 25:581-584.

*Lamarsh J. 1983. Introduction to nuclear engineering. 2nd ed. Reading, MA: Addison-Wesley Publishing Company, 177-188.

*Langham W. 1959. Physiology and toxicology of plutonium-239 and its industrial medical control. Health Phys 2:172-185.

*Langham W, Bassett S, Harris P, et al. 1980. Distribution and excretion of plutonium administered intravenously to man. Health Phys 38:1031-1060.

*Larsen R, Oldham R, Bhattacharyya M, et al. 1981. Plutonium retention in mice and rats after gastrointestinal absorption. Radiat Res 87:37-49.

Larson H. 1980. Factors in controlling personnel exposure to radiations from external sources. In: Plutonium handbook: A guide to technology. Vol I, II. La Grange Park, IL:
Society, 845-857.
The American Nuclear

*Leggett R. 1985. A model of the retention, translocation and excretion of systemic Pu. Health Phys 49:1115-1137.

*Leggett R, Eckerman K. 1987. A method for estimating the systemic burden of Pu from urinalyses. Health Phys 52:337-346.

8. REFERENCES

*Leonard B. 1980. Properties of plutonium isotopes. In: Plutonium handbook: A guide to the technology. Vol I, II. La Grange Park, IL: The American Nuclear Society, l-8.

*Little C, Whicker F. 1978. Plutonium distribution in Rocky Flats soil. Health Phys 34:451-457.

*Livens F, Baxter M. 1988. Particle size and radionuclide levels in some West Cumbrian soils. Sci Total Environ 70:1-17.

*Liverman .I, Yoder R, Wrenn M, et al. 1974. Plutonium and other transuranium elements: sources, environmental distribution and biomedical effects. A compilation of testimony presented before an EPA hearing board, December 10-11, 1974. U.S. Atomic Energy Commission, Division of Biomedical Effects, Washington, D.C. WASH-1359.

*Lloyd R, Atherton D, McFarland S, et al. 1976. Studies of injected 237Pu(IV) citrate in beagles. Health Phys 30:47-52.

*Lloyd R, McFarland S, Atherton D, et al. 1978a. Plutonium retention, excretion, and distribution in juvenile beagles soon after injection. Radiat Res 75:633-641.

*Lloyd R, McFarland S, Atherton D, et al. 1978b. Early retention of 237Pu+239Pu in mature beagles. Health Phys 35:211-215.

*Lloyd R, Boseman J, Taylor G et al. 1978~. Decorporation from beagles of a mixture of monomeric and particulate plutonium using Ca-DTPA and Zn-DTPA: Dependence upon frequency of administration. Health Phys 35:217-227.

*Lloyd R, Jones C, Taylor G, et al. 1984. Plutonium-237 and 239Pu retention in a St. Bernard. Health Phys 47:629-631.

Loutit J. 1977. Tumours and viruses in mice injected with plutonium. Nature 266:355-357.

Loutit J, Carr T. 1978. Lymphoid tumours and leukaemia induced in mice by bone-seeking radionuclides. Int J Radiat Biol Relat Stud Phys Chem Med 33:245-264.

Loutit J, Sansom J, Carr T. 1976. The pathology of tumors induced in Harwell mice by 239Pu and 226Ra. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 505-536.

*Lundgren D, Damon E, Die1 J, et al. 1981. The deposition, distribution and retention of inhaled 239PuO2 in the lungs of rats with pulmonary emphysema. Health Phys 40:231-235.

8. REFERENCES

*Lundgren D, Hahn F, Rebar A, et al. 1983. Effects of the single or repeated inhalation exposure of Syrian hamsters to aerosols of plutonium-239 dioxide. Int J Radiat Biol Relat Stud Phys Chem Med 43:1-18.

Lundgren D, Gillett N, Hahn F, et al. 1985. Repeated inhalation exposure of mice to aerosols of 239PuO2. IV. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-114.

*Lundgren D, Gillett N, Hahn F, et al. 1987. Effects of protraction of the alpha dose to the lungs of mice by repeated inhalation exposure to aerosols of plutonium-239 oxide. Radiat Res 111:201-224.

*Liining K, Frolen H, Nilsson A. 1976a. Dominant lethal tests of male mice given 239Pu salt injections. In: Biological and environmental effects of low-level radiation. Vol 1. Vienna: International Atomic Energy Agency, 39-49.

*Liining K, Frolen H, Nilsson A. 1976b. Genetic effects of 239Pu salt injections in male mice. Mutat Res 34:539-542.

*Mahlum D, Hess J. 1978. Alcohol and radionuclide metabolism. Part I: Biomedical sciences. 1977 Annual Report to U.S. Department of Energy, Washington, DC, by Battelle Pacific Northwest Laboratories, Richland, WA.

*Mahlum D, Sikov M. 1969a. Physicochemical state as a determinant of plutonium-238 toxicity in the rat. Health Phys 17:346-347.

*Mahlum D, Sikov M. 1969b. Skeletal changes produced by the administration of plutonium-239 and cerium-144 to weanling rats. In: Sikov M, Mahlum D, eds. Radiation biology of the fetal and juvenile mammal. Proceedings 9th Annual Hanford Biological Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA.

*Mahlum D, Sikov M. 1974. Distribution and toxicity of monomeric and polymeric 239-Pu in immature and adult rats. Radiat Res 60:7,5-88.

Mahlum D, Sikov M, Hungate F. 1976. Influence of temporal distribution of alpha dose in bone tumor induction. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 49-56.

Mancuso T, Stewart A, Kneale G. 1977. Radiation exposures of Hanford workers dying from cancer and other causes. Health Phys 33:369-385.

8. REFERENCES

Mancuso T, Stewart A, Kneale G. 1981. Analyses of Hanford data: Delayed effects of small doses of radiation delivered at slow-dose rates. In: Peto R, Schneiderman M, eds. Quantification of occupational cancer. Banbury report 9. Cold Spring Harbor, MI: Cold Spring Harbor Laboratory, 129-150.

*Martin J. 1986. Determination of 241Pu in low-level radioactive wastes from reactors. Health Phys 51:621-631.

Matsuoka 0, Kashima M, Joshima H, et al. 1972. Whole-body autoradiographic studies on plutonium metabolism as affected by its physico-chemical state and route of administration. Health Phys 22:713-722.

*Mays C, Lloyd R, Taylor G, et al. 1987. Cancer incidence and lifespan vs. alpha-particle dose in beagles. Health Phys 52:617-624.

*McInroy J, Kathren R, Swint M. 1989. Distribution of plutonium and americium in whole bodies donated to the United States transuranium registry. Radiat Protect-Dosimet 26:151-158.

McShane J, Dagle G, Park J. 1980. Pulmonary distribution of inhaled 239PuO2 in dogs. In: Sanders C, et al., eds. Pulmonary toxicology of respirable particles. 19th Annual Hanford Life Sciences Symposium, Richland, WA. U.S. Department of Energy, Washington, DC.

*Metivier H, Nolibe D, Masse R, et al. 1974. Excretion and acute toxicity of 239PuO2 in baboons. Health Phys 27:512-514.

Metivier H, Masse R, Nolibe D, et al. 1977. Effect of time on the determination of the clearance rates of insoluble plutonium 239 oxide. Health Phys 32:447-449.

*Metivier H, Masse R, Legendre N, et al. 1978a. Pulmonary connective tissue modifications induced by internal alpha irradiation. I. Effect of time and dose on alterations following inhalation of plutonium-239 dioxide aerosol in rat. Radiat Res 75:385-396.

*Metivier H, Nolibe D, Masse R, et al. 1978b. New data on toxicity and translocation of inhaled 239PuO2 in baboons. Health Phys 35:401-404.

*Metivier H, Masse R, Rateau G, et al. 1980a. Experimental study of respiratory contamination by a mixed oxide aerosol formed from the combustion of a plutonium magnesium alloy. Health Phys 38:769-776.

8. REFERENCES

Metivier H, Junqua S, Masse R, et al. 1980b. Pulmonary connective tissue modifications induced in the rat by inhalation of 239PuO2 aerosol. In: Sanders C, et al., eds. Pulmonary toxicology of respirable particles. 19th Hanford Life Sciences Symposium, Richland, WA. U.S. Department of Energy, Washington, DC.

Metivier H, Masse R, Lafuma J. 1983. Metabolism of plutonium introduced as tri-n-butylphosphate complex in the rat and removal attempts by DTPA. Health Phys 44:623-634.

*Metivier H, Wahrendorf J, Masse R. 1984. Multiplicative effect of inhaled plutonium oxide and benzo(a)pyrene on lung carcinogenesis in rats. Br J Cancer 50:215-21.

*Metivier H, Masse R, Wahrendorf J, et al. 1986. Combined effects of inhaled plutonium oxide and benzo(a)pyrene on lung carcinogenesis in rats. In: Thompson R, McHaffey J, eds. Life-span radiation effects studies in animals: What can they tell us? 22nd Hanford Life Sciences Symposium, Richland WA. U.S. Department of Energy, Washington, DC. NTIS no. DE87000490.

*Metz C, Waterbury G. 1962. The transuranium actinide elements. In: Kolthoff I, Elving P, eds. Treatise on analytical chemistry. Part II. Analytical chemistry of the elements. Vol 9. The transuranium actinide elements. New York: Interscience Publishers, 228-229.

Mewhinney J, Hahn F, Muggenburg B, et al. 1985. Toxicity of inhaled 238PuO2 in beagle dogs: A. Monodisperse 1.5 um AMAD particles. B. Monodisperse 3.0 um particles. XII. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. IMF-114.

*Mewhinney J, Hobbs C, McClellan R, et al. 1986. Toxicity of inhaled polydisperse of monodisperse aerosols of 238PuO2 in Syrian hamsters. IV. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-115.

*Mewhinney J, Gillett, H, Muggenburg, B, et al. 1987a. Toxicity of 238PuO2 in beagle dogs: A. Monodisperse l.S-pn amad particles. B.

Monodisperse 3.0-pm AMAD particles. XIV. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-120.

*Mewhinney J, Edison A, Wong V. 1987b. Effect of wet and dry cycles on dissolution of relatively insoluble particles containing Pu. Health Phys 53:377-384.

8. REFERENCES

*Meyer G. 1976. Preliminary data on the occurrence of transuranium nuclides in the environment at the radioactive waste burial site Maxey Flats, Kentucky. IAEA-SM-199/105. In: Transuranium nuclides in the environment. Proceedings of a symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 231-270.

Miller S, Bowman B. 1983. Tissue, cellular, and subcellular distribution of 241Pu in the rat testis. Radiat Res 94:416-426.

*Miller S, Jee W, Smith J, et al. 1986. Tissue characteristics of high- and low-incidence plutonium-induced osteogenic sarcoma sites in life-span beagles. in: Thompson R, McHaffey J, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings 22nd Hanford Life Sciences Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DE87000490.

*Miller S, Bruenger F, Williams F. 1989. Influence of,age at exposure on concentrations of 239Pu in beagle gonads. Health Phys 56:485-491.

*Miyake Y, Sugimura Y. 1976. The plutonium content of Pacific Ocean waters. IAEA-SM-199/22. In: Transuranium nuclides in the environment. Proceedings of the symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 91-105.

Moghissi A, Carter M. 1975. Comments on "comparative distribution and excretion of 237Pu and 239Pu nitrates in beagle dogs." Health Phys 28:825-826.

*Moores S, Talbot R, Evans N, et al. 1986. Macrophage depletion of mouse lung following inhalation of plutonium-239 dioxide. Radiat Res 105:387-404.

*Morin M, Nenot J, Lafuma J. 1972. Metabolic and therapeutic study following administration to rats of 238Pu nitrate--A comparison with 239Pu. Health Phys 23:475-480.

*Morris J, Winn L. 1978. Effects of inhaled 239PuO2 on the primary immune response of beagle dogs. Part I: Biomedical sciences. 1977 Annual report to U.S. Department of Energy, Washington, DC, by Pacific Northwest Laboratory, Richland, WA. PNL-2500.

*Muggenburg B, Wolff R, Mauderly J, et al. 1986. Cardiopulmonary function of dogs with plutonium-induced chronic lung injury. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-115.

8. REFERENCES

*Muggenburg B, Guilmette R, Hahn F, et al. 1987a. Toxicity of inhaled 239PuO2 in beagle dogs. A. Monodisperse 0.75 pm AMAD particles. B.

Monodisperse 1.5 pm AMAD particles. C. Monodisperse 3.0 pm AMAD particles. X. Annual Report to U.S. Department of Energy, Washington. DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-120.

*Muggenburg B, Hahn F, Gillett N, et al. 1987b. Toxicity of 239PuO2 inhaled by aged beagle dogs. IX. Annual Report to U.S. Department of Energy, Washington, DC, by Inhalation Toxicology Research Institute, Albuquerque, NM. Report No. LMF-120.

*Muggenburg B, Wolff R, Mauderly J, et al. 1988. Cardiopulmonary function of dogs with plutonium-induced chronic lung injury. Radiat Res 115:314-324.

National Research Council. 1976. Health effects of alpha-emitting particles in the respiratory tract. Report of ad hoc committee-on "hot particles" of the advisory committee on the biological effects of ionizing radiations. National Academy of Sciences, National Research Council, Washington, D.C.

*NAS/NRC. 1989. Biologic markers in reproductive toxicology. National Academy of Sciences/National Research Council. Washington, DC: National Academy Press, 15-35.

*NCRP. 1984. Radiological assessment: Predicting the transport, bioaccumulation, and uptake by man of radionuclides released to the environment. NCRP Report No. 76. Bethesda, MD: National Council on Radiation Protection and Measurements, 73-85, 127-152.

*NCRP. 1985. A handbook of radioactivity measurements procedures. 2nd ed. NCRP Report No. 58. Bethesda, MD: National Council on Radiation Protection and Measurements, 217-250.

*NCRP. 1987. Ionizing radiation exposure of the population of the United States. Recommendations of the NCRP. NCRP Report No. 93. Bethesda, MD: National Council on Radiation Protection and Measurements, l-60.

*NEA/OECD. 1981. The environmental and biological behaviour of plutonium and some other transuranium elements. Nuclear Energy Agency, OECD, Paris.

*NEA/OECD. 1983. Dosimetry aspects of exposure to radon and thoron daughter products. Nuclear Energy Agency, OECD, Paris.

8. REFERENCES

*Nelson I, Thomas V. 1977. Plutonium in human lung in the Hanford environs. Presented 4th International Congress International Radiation Protection Association, Paris, France. BNWL-SA-5855. Richiand, WA: Battelle Pacific Northwest Laboratories.

*Nelson D, Larson R, Penrose W. 1987. Chemical speciation of plutonium in natural waters. In: Pinder, J, et al., eds. Environmental research on actinide elements. Office of Science and Technical Information. U.S. Department of Energy, Springfield, VA. NTIS no. DE-86008718.

*Nenot J, Stather J. 1979. The toxicity of plutonium, americium and curium. A report prepared under contract for the Commission of,the European Communities within its Research and Development Programme on “Plutonium Recycling in Light Water Reactors." New York: Pergammon Press, 1-9.

*Nenot J, Masse R, Morin M, et al. 1972. An experimental comparative study of the behaviour of 237Np, 238Pu, 239Pu, 241Am and 242Cm in bone. Health Phys 22:657-665.

*Nero A, Jr. 1979. Instrumentation for monitoring plutonium in the environment. Nuclear Safety 20:280-290.

*Nielson J, Beasley T. 1980. Radiochemical determination of plutonium for radiological purposes. In: Wick 0, ed. Plutonium handbook: A guide to the technology. Vol 2. The American Nuclear Society, Illinois, 921-933.

Nolibe D, Discour M, Masse R, et al. 1980. The effects of immune modulation on plutonium dioxide lung carcinogenesis in the rat. In: Sanders C, et al., eds. Pulmonary toxicology of respirable particles. 19th Hanford Life Sciences Symposium, Richland, WA. U.S. Department of Energy, Washington, DC.

Nolibe D, Masse R, Lafuma J. 1981. The effect of neonatal thymectomy on lung cancers induced in rats by plutonium dioxide. Radiat Res 87:90-99.

*Noshkin V, Wong K, Marsh K, et al. 1976. Plutonium radionuclides in the groundwaters at Enewetak Atoll. IAEA-SM-199/33. In: Transuranium nuclides in the environment. Proceedings of the symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 517-543.

*NRc . 1988. Nuclear Regulatory Commission. Code of Federal Regulations. 10 CFR 20.

8. REFERENCES

*Oakley W, Thompson R. 1956. Further studies on percutaneous absorption and decontamination of plutonium in rats. Biology research annual report to U.S. Department of Energy, Washington, DC, by Hanford Atomic Products Operation, Richland. Washington. Report HW-41500.

*Okabayashi H, Watanabe H. 1973. Concentration of plutonium in Japanese human bone. J Radiat Res 14:363-368.

*Okabayashi H, Watanabe H, Takizawa Y. 1978. Measurement of plutonium in Japanese human organs. J Radiat Res 19:62-69.

*OTA. 1990. Neurotoxicity, identifying and controlling poisons of the nervous system, new developments in neuroscience. Office of Technology Assessment, Congress of the United States.

Paglia D. 1968. Hematopathologic surveys of kangaroo rats (Dioodomvs microns) populating plutonium contaminated regions of the Nevada test site. Health Phys 15:493-498.

Park J, Willard D, Marks S, et al. 1962. Acute and chronic toxicity of inhaled plutonium in dogs. Health Phys 8:651-657.

Park J, Clarke W, Bair W. 1964. Chronic effects of inhaled plutonium in dogs. Health Phys 10:1211-1217.

Park J, Howard E, Stuart B, et al. 1970. Cocarcinogenic studies in pulmonary carcinogenesis. In: Nettesheim P, et al., eds. Morphology of experimental respiratory carcinogenesis. Symposium Series 21. Washington, D.C.: U.S. Atomic Energy Commission, 417-436.

*Park J, Bair W, Busch R. 1972. Progress in beagle dog studies with transuranium elements at Battelle-Northwest. Health Phys 22:803-810.

Park J, Lund J, Ragan H, et al. 1976. Bone tumors induced by inhalation of plutonium-238 dioxide in dogs. Recent Results Cancer Res 54:17-35.

Park J, Case A, Catt D, et al. 1978. Inhaled plutonium oxide in dogs. Part I: Biomedical sciences. 1977 Annual Report to U.S. Department of Energy, Washington, DC, by Pacific Northwest Laboratory, Richland, WA. PNL-2500.

*Park J, Apley G, Case A, et al. 1985. Inhaled plutonium oxide in dogs. Annual Report to U.S. Department of Energy, Washington, DC, by Pacific Northwest Laboratory, Richland, WA.

8. REFERENCES

Park J, Dagle G, Ragan H, et al. 1986. Current status of life-span studies with inhaled plutonium in beagles at Pacific Northwest Laboratory. In: Thompson R, Mahaffey J, eds. Life-span radiation effects studies in animals: What can they tell us? Proceeding 22nd Hanford Life Sciences Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield VA. NTIS no. DE98000490.

*Park J, Buschbom R, Dagle G, et al. 1988. Inhaled plutonium oxide in dogs. Part 1. Biomedical sciences. 1987 Annual Report to U.S. Department of Energy, Office of Energy Research by Pacific Northwest Laboratory, Richland, WA. PNL-6500-Part 1. NTIS no. DE88-011885.

*Perkins R, Thomas C. 1980. Worldwide fallout. In: Hanson W, ed. Transuranic elements in the environment. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DOE/TIC-22800.

*Pillai K, Mathew E. 1976. Plutonium in the aquatic environment: Its behavior, distribution and significance. IAEA-SM-199/27. In: Transuranium nuclides in the environment. Proceedings of the symposium on transuranium nuclides in the environment. Vienna: International Atomic Energy Agency, 25-45.

*Pinder J III, Adrian0 D, Ciravolo T, et al. 1987. The interception and retention of 238Pu deposition by orange trees. Health Phys 52:707-715.

*Popplewell D, Ham G, Dodd N, et al. 1988. Plutonium and Cs-137 in autopsy tissues in Great Britain. Sci Total Environ 70:321-334.

*Prise K, Davies S, Michael B. 1987. The relationship between radiation-induced DNA double-strand breaks and cell kill in hamster V79 fibroblasts irradiated with 250 kVp X-rays, 2.3 MeV neutrons or 238Pu alpha-particles. Int J Radiat Biol 52:893-902.

*Purrott R, Edwards A, Lloyd D, et al. 1980. The induction of chromosome aberrations in human lymphocytes by in vitro irradiation with alpha-particles from plutonium-239. Int J Radiat Biol 38:277-284.

*Ragan H. 1977. Body-iron stores and plutonium metabolism. In: Drucker H, Wildung R, eds. Biological implications of metals in the environment. Proceedings 15th Hanford Life Sciences Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA.

8. REFERENCES

*Ragan H, Buschbom R, Park J, et al. 1986, Hematologic effects of inhaled plutonium in beagles. In: Thompson R, McHaffey J, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings 22nd Hanford Life Sciences Symposium, Rlchland WA. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DE87000490.

*Reyes M, Wilkinson G, Tietjen G, et al. 1983. Case-control study of brain tumors among white males employed at the Rocky Flats plant. Report to U.S. Department of Energy by Los Alamos National Laboratory, Los Alamos, NM. LA-9804-MS.

Reyes M, Wilkinson G, Tietjen G, et al. 1984. Brain tumors at a nuclear facility. J Occup Med 26:721-724.

*Robertson J, Raju M. 1980. Sudden reversion to normal radiosensitivity to the effects of x-irradiation and plutonium-238 alpha particles by a radioresistant rat-mouse hybrid cell line. Radiat Res 83:197-204.

*Rowland R, Durbin P. 1976. Survival, causes of death, and'estimated tissue doses in a group of human beings injected with plutonium. In: Webster S, ed.. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 329-341.

Rundo J, Holtzman R. 1976. Comparison of the late excretion of 226Ra and 239Pu by man. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 497-504.

*Sanders C. 1973a. Cocarcinogenesis of 239PuO2 with chrysotile asbestos or benzpyrene in the rat abdominal cavity. In: Sanders C, et al., eds. Radionuclide carcinogenesis. Symposium Series 29. Washington, D.C.: U.S. Atomic Energy Commission, 138-153.

*Sanders C. 1973b. Carcinogenicity of inhaled plutonium-238 in the rat. Radiat Res 56:540-553.

*Sanders C. 1974. Rat mammary neoplasia following deposition of plutonium. Health Phys 27:592-593.

*Sanders C. 1975a. Effects of PuO2 particles deposited in the lung following intraperitoneal injection. Health Phys 28:84-86.

*Sanders C. 1975b. Dose distribution and neoplasia in the lung following intratracheal instillation of 239PuO2 and asbestos. Health Phys 28:383-386.

*Sanders C. 1977. Inhalation toxicology of 238PuO2 and 239PuO2 in Syrian golden hamsters. Radiat Res 70:334-344.

8. REFERENCES

Sanders C. 1978. Effects of repeated exposures to 239PuO2. Part I: Biomedical sciences. 1977 Annual Report to U.S. Department of Energy, Washington, DC, by Pacific Northwest Laboratory, Richland, WA. PNL-2500.

*Sanders C, Adee R. 1970. Ultrastructural localization of inhaled 239PuO2 particles in alveolar epithelium and macrophages. Health Phys 18:293-295.

*Sanders C, Jackson T. 1972. Induction of mesotheliomas and sarcomas from "hot spots" of 239PuO2 activity. Health Phys 22:755-759.

*Sanders C, Mahaffey J. 1979. Carcinogenicity of inhaled air-oxidized plutonium-239 dioxide in rats. Int J Radiat Biol Relat Stud Phys Chem Med 35:95-98.

*Sanders C, Mahaffey J. 1981. Inhalation carcinogenesis of repeated exposures to high-fired 239PuO2 in rats. Health Phys 41:629-644.

*Sanders C, Mahaffey J. 1983. Action of vitamin C on pulmonary carcinogenesis from inhaled 239PuO2. Health Phys 45:794-798.

*Sanders C, Dagle G, Cannon W, et al. 1976. Inhalation carcinogenesis of high-fired plutonium-239 dioxide in rats. Radiat Res 68:349-360.

*Sanders C, Dagle G, Cannon W, et al. 1977. Inhalation carcinogenesis of high-fired plutonium-238 dioxide in rats. Radiat Res 71:528-546.

*Sanders C, Cannon W, Powers G. 1978. Lung carcinogenesis induced by inhaled high-fired oxides of beryllium and plutonium. Health Phys 35:193-199.

Sanders C, Mahaffey J, McDonald K, et al. 1985. Low-level 239PuO2 lifespan studies. Annual Report to U.S. Department of Energy, Washington, DC, by Pacific Northwest Laboratory, Richland, WA.

*Sanders C, McDonald K, Killand B, et al. 1986. Low-level inhaled-239Pu02 life-span studies in rats. In: Thompson R, McHaffey J, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings 22nd Hanford Life Sciences Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DE87000490.

*Sanders C, McDonald K, Mahaffey J. 1988. Lung tumor response to inhaled Pu and its implications for radiation protection. Health Phys 55:455-462.

8. REFERENCES

*Schell W, Lowman F, Marshall R. 1980. Geochemistry of transuranic elements at Bikini Atoll. In: Hanson W, ed. Transuranic elements in the environment. Technical Information Center, U.S.Department of Energy, Springfield, VA. NTIS no. DOE/TIC-22800.

*Schofield G. 1980. Biological control in a plutonium production facility. Br J Radio1 53:398-409.

*Schofield G, Howells H, Ward F, et al. 1974. Assessment and management of a plutonium contaminated wound case. Health Phys 26:541-554.

Schofield R, Lord B, Humphreys E, et al. 1986. Effects of plutonium-239 on hemopoiesis. I. Quantitative and qualitative changes in CFU-S in different regions of the mouse femur and vertebrae. Int J Radiat Biol 49:1021-1029.

*Searle A, Beechey C, Green D, et al. 1976. Cytogenetic effects of protracted exposures to alpha-particles from plutonium-239 and to gamma-rays from cobalt-60 compared in male mice. Mutat Res 41:297-310.

*Searle A, Beechey C, Green D, et al. 1980. Comparative effects of protracted exposures to 6OCo gamma-radiation and 239Pu alpha-radiation on breeding performance in female mice. Int J Radiat Biol 37:189-200.

*Searle A, Beechey C, Green D, et al. 1982. Dominant lethal and ovarian effects of plutonium-239 in female mice. Int J Radiat Biol 42:235-244.

Sikov M, Mahlum D. 1968. Cross-placental transfer of selected actinides in the rat. Health Phys 14:205-208.

*Sikov M, Mahlum D. 1976. Influence of age and physicochemical form on the effects of 239Pu on the skeleton of the rat. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 33-47.

*Sikov M, Swicker G, Hess J, et al. 1978a. Late effects of perinatally administered plutonium. In: Mahlwn D, et al., eds. Developmental toxicology of energy-related pollutants. Proceedings 17th Hanford Biology Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA.

*Sikov M, Andrew F, Berstine R, et al. 1978b. Cross-placental transfer of plutonium 239 in gravid baboons. Part 1. Annual Report to U.S. Department of Energy, Washington, *DC,* by Pacific Northwest laboratory, Richland, WA. PNL-2500.

8. REFERENCES

*Sill C. 1975. Some problems in measuring plutonium in the environment. In: Healy J, ed. Plutonium--health implications for man. New York: Pergammon Press, 619-626.

*Singh N, Wrenn M. 1988. Determinations of actinides in biological and environmental samples. Sci Total Environ 70:187-204.

Smith D, Anderson E, Prine J, et al. 1976. Biological effect of focal alpha radiation on the hamster lung. In: Biological and environmental effects of low-level radiation. Vol 2. International Atomic Energy Agency, Vienna, 121-129.

Smith D, Thomas R, Anderson E. 1980. Respiratory-tract carcinogenesis induced by radionuclides in the Syrian hamster. In: Sanders C, et al., eds. Pulmonary toxicology of respirable particles. 19th Hanford Life Sciences Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA.

*Smith J, Lloyd R, Atherton D, et al. 1976. The early retention and distribution of monomeric 237Pu(IV) and 239Pu(IV) in C57BL/Do mice. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 7-20.

*Smith J, Taylor G, Mays C, ***et*** al. 1978. The early retention of monomeric 237Pu(IV)- and 239Pu(IV)-citrate in C57BL/DO and BALB/CJ mice. Radiat Res 75:502-509.

*Smith J, Miller S, Jee W. 1984. The relationship of bone marrow type and microvasculature to the microdistribution and local dosimetry of plutonium in the adult skeleton. Radiat Res 99:324-335.

*Stather J, Harrison J, Smith H, et al. 1980. The influence of fasting and valence on the gastrointestinal absorption of plutonium in hamsters and rabbits. Health Phys 39:334-338.

*Stather J, Harrison J, David A, et al. 1981. The gastrointestinal absorption of plutonium in the hamster after ingestion at low concentrations in drinking water. Health Phys 41:780-783.

*Stevens W, Bruenger F, Stover B. 1968. In vivo studies on the interaction of Pu(IV) with blood constituents. Radiat Res 33:490-500.

Stevens W, Stover B, Atherton D, et al. 1975. Distribution and excretion of three chemical species of 239Pu(IV) in the beagle. Health Phys 28:387-394.

8. REFERENCES

*Stevens W, Atherton D, Jee W, et al. 1976. induction of osteogenic sarcoma by polymeric plutonium (239PuIV) in beagles. In: Webster S, ed. The health effects of plutonium and radium. Salt Lake City, UT: J.W. Press, 81-95.

*Stover B, Atherton D, Keller N. 1959. Metabolism of Pu239 in adult beagle dogs. Radiat Res 10:130-147.

*Stover B, Atherton D, Bruenger F, et al. 1962. Further studies of the metabolism of Pu239 in adult beagles. Health Phys 8:589-597.

*Stover B, Bruenger F, Stevens W. 1968a. The reaction of Pu(IV) with the iron transport system in human blood serum. Radiat Res 33:381-394.

*Stover B, Atherton D, Bruenger F, et al. 1968b. Plutonium-239 in liver, spleen and kidneys of the beagle. Health Phys 14:193-97.

Stover B, Atherton D, Buster D. 1971. Protracted hepatic, splenic and renal retention of 239Pu in the beagle. Health Phys 20:369-374.

Stroud A. 1977. Chromosome aberrations induced in Syrian hamster lung cells by inhaled 238Pu02-Zr02 particles. Radiat Res 69:583-590.

*Sullivan M, Hackett P, George A, et al. 1960. Irradiation of the intestine by radioisotopes. Radiat Res 13:343-355.

*Sullivan M, Miller B, Gorham L. 1983. Nutritional influences on plutonium absorption from the gastrointestinal tract of the rat. Radiat Res 96:580-591.

*Sullivan M, Ruemmler P. 1988. Absorption of 233U, 237Np, 238Pu, 241Am and 244Cm from the gastrointestinal tracts of rats fed an iron-deficient diet. Health Phys 54:311-316.

*Sullivan M, Miller B, Goebel J. 1984. Gastrointestinal absorption of metals (chromium-51, zinc-65, technetium-99m, cadmium-log, tin-113, promethium-147 and plutonium-238) by rats and swine. Environ Res 35:439-453.

*Sullivan M, Reummler P, Buschbom R. 1986. Influence of iron on plutonium absorption by the adult and neonatal rat. Toxicol Appl Pharmacol 85:239-247.

*Sullivan M, Garland T, Cataldo D, et al. 1980. Absorption of plutonium from the gastrointestinal tract of rats and guinea pigs after ingestion of alfalfa containing 238Pu. Health Phys 38:215-221.

8. REFERENCES

*Svoboda V, Kotaskova Z. 1982. Intensified proliferative activity of the CFU-S in vertebral bone marrow of 239Pu-treated mice as one of the factors involved in the induction of granulocytic leukemia. Neoplasma 29:719-726.

*Svoboda V, Kotaskova Z. 1983. Radiosensitivity and proliferative activity of vertebral CFU-S surviving in mice injected with oncogenic activities of plutonium-239 and americium-241. J Hyg Epidemiol Microbial Immunol 27:329-335.

*Svoboda V, Kotaskova 2, Lenger V, et al. 1979. Effect of 239Pu on mouse hemopoietic stem cells in different types of bone marrow cavities. Radiat Environ Biophys 16:339-345.

*Svoboda V, Klener V, Bubenikova D, et al. 1980a. Terminal hematological changes in mice bearing osteosarcomas induced by plutonium-239. Neoplasma 27:567-574.

*Svoboda V, Klener V, Bubenikova D et al. 1980b. Bone sarcomas in 239Pu-treated mice. Neoplasma 27:3-10.

*Svoboda V, Bubenikova D, Kotaskova Z. 1981. Myeloid leukemia 239Pu-treated mice. J Cancer Res Clin Oncol 100:255-262.

*Svoboda V, Sedlak A, Bubenikova D, et al. 1982a. Biological effects of bone-seeking alpha emitters with respect to the risk of internal contamination in man. Czech Med 5:80-89.

Svoboda V, Bubenikova D, Kotaskova Z. 1982b. Some quantitative micromorphological characteristics of granulocytic leukemia in 239Pu-injected mice and untreated controls. Neoplasma 29:175-182.

*Svoboda V, Sedlak A, Bubenikova D, et al. 1985. Self-renewal capacity of murine hemopoietic stem cells under internal contamination with 239Pu and 241Am. Radiat Environ Biophys 24:203-209.

*Svoboda V, Sedlak A, Kypenova H, et al. 1987. Long-term effects of low-level 239Pu contamination on murine bone-marrow stem cells and their progeny. Int J Radiat Biol 52:517-526.

Svoboda V, Bubenikova D, Sedlak A. 1988. Effect of plutonium-239 on the mitotic activity of mouse bone marrow cells. Radiat Environ Biophys 27:79-85.

*Takizawa Y. 1982. Plutonium in Japanese tissues. J Radiat Res 23:198-203.

8. REFERENCES

*Talbot R, Moores S. 1985. The development and interlobar distribution of plutonium-induced pulmonary fibrosis in mice. Radiat Res 103:135-148.

*Talbot R, Morgan A, Moores S, et al. 1987. Preliminary studies of the interaction between 239PuO2 and cigarette smoke in the mouse lung. Int J Radiat Biol 51:1101-1110.

*Tawn E, Hall J, Schofield G. 1985. Chromosome studies in plutonium workers. Int J Radiat Bioi 47:599-610.

*Taylor D. 1973. Chemical and physical properties of plutonium. In: Hodge H, et al., eds. Uranium, plutonium - transplutonic elements. New York: Springer-Verlag, 323-347.

*Taylor D. 1977. The uptake, retention and distribution of plutonium-239 in rat gonads. Health Phys 32:29-31.

Taylor D. 1980. Mobilization of internally deposited plutonium from the rat by pregnancy and lactation. Int J Radiat Biol 38:357-360.

Taylor D. 1986. The comparative carcinogenicity of 239Pu, 241Am, and 244Cm in the rat. In: Thompson R, McHaffey J, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings 22nd Hanford Life Sciences Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DE87000490.

*Taylor G, Christensen W, Jee W, et al. 1962. Anatomical distribution of fractures in beagles injected with Pu239. Health Phys 8:609-613.

*Taylor G, Gardner P, Mays C, et al. 1981a. Incidence of plutonium-induced bone cancer in neutered mice. Cancer Res 41:971-973.

Taylor G, Thurman G, Mays C, et al. 1981b. Plutonium-induced osteosarcomas in the St. Bernard. Radiat Res 88:180-186.

*Taylor G, Mays C, Lloyd R, et al. 1983. Comparative toxicity of radium-226, plutonium-239, americium-241, californium-249, and californium-252 in C57BL/Do black and albino mice. Radiat Res 95:584-601.

*Taylor G, Mays C, Wrenn M, et al. 1986. Incidence of liver tumors in beagles with body burdens of 239Pu or 241Am. In: Thompson R, McHaffey J, eds. Life-span radiation effects studies in animals: What can they tell us? Proceedings 22nd Hanford Life Sciences Symposium, Richland, WA. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DE87000490.

8. REFERENCES

Temple L. Willard D, Smith V, et al. 1957. Lung tumors for deposition of particulate material. Biology Research Annual Report 1956 to U.S. Department of Energy, Washington, DC, by Hanford Atomic Products Operation, Richland, WA. Report No. HW-47500.

*Thacker J, Stretch A, Goodhead D. 1982. The mutagenicity of alpha particles from plutonium-238. Radiat Res 92:343-352.

Thompson R, Wachholz B. 1980. Biological effects of transuranic elements in the environment: Human effects and risk estimates. In: Hanson W, ed. Transuranic elements in the environment. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DOE/TIC-22800.

Thompson R, Cross F, Dagle G, et al. 1986. DOE life-span radiation effects studies at Pacific Northwest Laboratory. In: Thompson R, Mahaffey J, eds. Life-span radiation effects studies in animals: What can they tell us? Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. CONF-830851.

Thurman G, Mays C, Taylor G, et al. 1971. Growth dynamics of beagle osteosarcomas. Growth 35:119-125.

*Todd R, Logan R. 1968. Plutonium-237 for metabolic studies: Its preparation and use. Int J Appl Radiat Isot 19:141-145.

*Toohey R, Bhattacharyya M, Oldham R, et al. 1984. Retention of plutonium in the beagle after gastrointestinal absorption. Radiat Res 97:373-379.

*UNSCEAR. 1982. United Nations Scientific Committee on the Effects of Atomic Radiation. Ionizing radiation: Sources and biological effects. New York: United Nations.

Valle C, Pepin G, Pasquier C, et al. 1977. Variation of hepatic mitochondrial nucleotides in rats contaminated with plutonium-239. Curr Top Radiat Res Q 12:483-493.

*VIEW Database. 1989. Agency for Toxic Substances and Disease Registry (ATSDR), Office of External Affairs, Exposure and Disease Registry Branch, Atlanta, GA. June 29, 1989. (Map based on VIEW Database, June 12, 1989.)

*Voelz G, Hempelmann L, Lawrence J, et al. 1979. A 32-year medical follow-up of Manhattan project plutonium workers. Health Phys 37:445-485.

8. REFERENCES

Voelz G, Wilkinson G, Acquavelia J, et al. 1982. A review of epidemiologic studies at Los Alamos National Laboratory. Los Alamos, NM: Los Alamos National Laboratory. LA-UR-82-974. NTIS no. DE82-014065.

*Voelz G, Wilkinson G, Healy J, et al. 1983a. Mortality study of Los Alamos workers with higher exposures to plutonium. Los Alamos, NM: Los Alamos National Laboratory. LA-UR-83-95. NTIS no. DE83-006058.

*Voelz G, Wilkinson G, Acquavella J, et al. 1983b. An update of epidemiologic studies of plutonium workers. Health Phys 44 supp1:493-503.

*Voelz G, Grier R, Hempelmann L. 1985. A 37-year medical follow-up of Manhattan project Pu workers. Health Phys 48:249-259.

*Volchok H, Knuth R, Kleinman M. 1974. The respirable fraction of Sr90, Pu239 and Pb in surface air. USAEC Report HASL-278. U.S. Atomic Energy Commission, Washington, D.C.

*Volchok H, Schonberg M, Toonkel L. 1977. Plutonium concentrations in air near Rocky Flats. Health Phys 33:484-485.

*Volf v. 1980. Influence of cadmium and copper on the distribution pattern of plutonium in the rat. J Toxicol Environ Health 6:493-501.

*Walker W, Kirouac G, Rourke F. 1977. Chart of the nuclides. 12th ed. Knolls Atomic Power Laboratory, Schnectady, NY. General Electric Company.

*Weast R. 1980. CRC handbook of chemistry and physics. Physical constants of inorganic compounds and table of isotopes. Boca Raton, FL: CRC Press, Inc., B107-108, B112-113.

Weeks M, Oakley W. 1954. Absorption of plutonium through the living skin of the rat. Biology Research Annual Report 1953 to U.S. Atomic Energy Commission, Washington, DC, by Hanford Atomic Products Operation, Richland, WA. Report HW 30437.

*Weeks M, Oakley W. 1955. Percutaneous absorption of plutonium solutions in rats. Biology Research Annual Report 1954 to U.S. Atomic Energy Commission, Washington, DC, by Hanford Atomic Products Operation, Richland, WA. Report HW 35917.

*Weeks M, Ballou J, Thompson R. 1956. Effect of chemical and physical state on gastrointestinal absorption of plutonium. Biology Research Annual Report 1955 to U.S. Atomic Energy Commission, Washington, DC, by Hanford Atomic Products Operation, Richland, WA. Report HW 41500.

8. REFERENCES

*Weiss J, Walburg H. 1978. Influence of the mass of administered plutonium on its cross-placental transfer in mice. Health Phys 35:773-777.

*Welleweerd J, Wilder M, Carpenter S, et al. 1984. Flow cytometric determination of radiation-induced chromosome damage and its correlation with cell survival. Radiat Res 99:44-51.

*WHO . 1983. Environmental health criteria 25: Selected radionuclides. World Health Organization, Geneva, 169-229.

*Wildung R, Garland T. 1980. The relationship of microbial processes to the fate and behavior of transuranic elements in soils, plants, and animals. In: Hanson W, ed. Transuranic elements in the environment. Technical Information Center, U.S. Department of Energy, Springfield, VA. NTIS no. DOE/TIC-22800.

*Wildung R, Garland T, Rogers J. 1987. Plutonium interactions with soil microbial metabolites: Effect on plutonium sorption by soil. In: Pinder J, et al., eds. Environmental research on actinide elements. U.S. Department of Energy, Washington, DC.

*Wilkinson G, Tietjen G, Wiggs L, et al. 1987. Mortality among plutonium and other radiation workers at a plutonium weapons facility. Am J Epidemiol 125:231-250.

*Wrenn M, Cohen N. 1977. Determination of Pu-239, 240 tissue concentrations in nonoccupationally exposed residents of New York City. COO-2968-l. Institute of Environmental Medicine, New York University Medical Center, New York.

*Windholz M. 1983. The Merck index. 10th ed. Rahway, NJ: Merck and Co., Inc., 1087.

*Wronski T, Smith J, Jee W. 1980. The microdistribution and retention of injected 239Pu on trabecular bone surfaces of the beagle: Implications for the induction of osteosarcoma. Radiat Res 83:74-89.

9. GLOSSARY

Absorbed Dose -- The mean energy imparted to the irradiated medium, per unit mass, by ionizing radiation. Units: gray (Gy) , rd.

Absorbed Fraction -- A term used in internal dosimetry. It is that fraction of the photon energy (emitted within a specified volume of material) which is absorbed by the volume. The absorbed fraction depends on the source distribution, the photon energy, and the size, shape and composition of the volume.

Absorption -- The process by which radiation imparts some or all of its energy to any material through which it passes.

> **Self-Absorption** -- Absorption of radiation (emitted by radioactive atoms) by the material in which the atoms are located; in particular, the absorption of radiation within a sample being assayed.

Absorption Coefficient -- Fractional decrease in the intensity of an unscattered beam of x or gamma radiation per unit thickness (linear absorption coefficient), per unit mass (mass absorption coefficient), or per atom (atomic absorption coefficient) of absorber, due to deposition of energy in the absorber. The total absorption coefficient is the sum of individual energy absorption processes. (See Compton Effect, Photoelectric Effect, and Pair Production.)

> **Linear Absorption Coefficient** -- A factor expressing the fraction of a beam of x or gamma radiation absorbed in a unit thickness of material. In the expression I-I,e-“X, I, is the initial intensity, I the intensity of the beam after passage through a thickness of the material x, and p is the linear absorption coefficient.
>
> **Mass Absorption Coefficient** -- The linear absorption coefficient per cm divided by the density of the absorber in grams per cubic centimeter. It is frequently expressed as p/p, where p is the linear absorption coefficient and p the absorber density.

Absorption Ratio, Differential -- Ratio of concentration of a nuclide in a given organ or tissue to the concentration that would be obtained if the same administered quantity of this nuclide were uniformly distributed throughout the body.

Activation -- The process of inducing radioactivity by irradiation.

Activity -- The number of nuclear transformations occurring in a given quantity of material per unit time. (See Curie.)

9. GLOSSARY

Activity Median Aerodynamic Diameter (AMAD) -- The diameter of a unitdensity sphere with the same terminal settling velocity in air as that of the aerosol particulate whose activity is the median for the entire aerosol.

Acute Exposure -- Exposure to a chemical for a duration of 14 days or less, as specified in the toxicological profiles.

Acute Radiation Syndrome -- The symptoms which taken together characterize a person suffering from the effects of intense radiation. The effects occur within hours or weeks.

Adsorption Coefficient (Koc) -- The ratio of the amount of a chemical adsorbed per unit weight of organic carbon in the soil or sediment to the concentration of the chemical in solution at equilibrium.

Adsorption Ratio (Kd) -- The amount of a chemical adsorbed by a sediment or soil (i.e., the solid phase) divided by the amount of chemical in the solution phase, which is in equilibrium with the solid phase, at a fixed solid/solution ratio. It is generally expressed in micrograms of chemical sorbed per gram of soil or sediment.

Alpha Particle -- A charged particle emitted from the nucleus of an atom. An alpha particle has a mass charge equal in magnitude to that of a helium nucleus; i.e., two protons and two neutrons and has a charge of +2.

Annihilation (Electron) -- An interaction between a positive and a negative electron in which they both disappear; their energy, including rest energy, being converted into electromagnetic radiation (called annihilation radiation} with two 0.51 Mev gamma photons emitted at an angle of 180° to each other.

Atomic Mass -- The mass of a neutral atom of a nuclide, usually expressed in terms of "atomic mass units." The "atomic mass unit" is one-twelfth the mass of one neutral atom of carbon-12; equivalent to 1.6604×10^{-24} gm. (Symbol: u)

Atomic Number -- The number of protons in the nucleus of a neutral atom of a nuclide. The "effective atomic number" is calculated from the composition and atomic numbers of a compound or mixture. An element of this atomic number would interact with photons in the same way as the compound or mixture. (Symbol: Z)

Atomic Weight -- The weighted mean of the masses of the neutral atoms of an element expressed in atomic mass units.

9. GLOSSARY

Auger Effect -- The emission of an electron from the extranuclear portion of an excited atom when the atom undergoes a transition to a less excited state.

Background Radiation -- Radiation arising from radioactive material other than that under consideration. Background radiation due to cosmic rays and natural radioactivity is always present. There may also be background radiation due to the presence of radioactive substances in building materials.

Becquerel (Bq) -- International System of Units unit of activity and equals one transformation (disintegration) per second. (See Units.)

Beta Particle -- Charged particle emitted from the nucleus of an atom. A beta particle has a mass and charge equal in magnitude to that of the electron. The charge may be either +l or -1.

Biologic Effectiveness of Radiation -- (See Relative Biological Effectiveness.)

Bone Seeker -- Any compound or ion which migrates in the body preferentially into bone.

Branching -- The occurrence of two or more modes by which a radionuclide can undergo radioactive decay. For example, radium C can undergo a or is- decay, ^{64}Cu can undergo β^-,β^+, or electron capture decay. An individual atom of a nuclide exhibiting branching disintegrates by one mode only. The fraction disintegrating by a particular mode is the "branching fraction" for that mode. The "branching ratio" is the ratio of two specified branching fractions (also called multiple disintegration).

Bremsstrahlung -- The production of electromagnetic radiation (photons) by the negative acceleration that a fast, charged particle (usually an electron) undergoes from the effect of an electric or magnetic field, for instance, from the field of another charged particle (usually a nucleus).

Cancer Effect Level (CEL) -- The lowest dose of chemical in a study, or group of studies, that produces significant increases in the incidence of cancer (or tumors) between the exposed population and its appropriate control.

Capture, Electron -- A mode of radioactive decay involving the capture of an orbital electron by its nucleus. Capture from a particular electron shell is designated as "K-electron capture," "L-electron capture," etc.

9. GLOSSARY

Capture, K-Electron -- Electron capture from the K shell by the nucleus of the atom. Also loosely used to designate any orbital electron capture process.

Carcinogen -- A chemical capable of inducing cancer.

Carcinoma -- Malignant neoplasm composed of epithelial cells, regardless of their derivation.

Cataract -- A clouding of the crystalline lens of the eye which obstructs the passage of light.

Ceiling Value (DL) -- A concentration of a substance that should not be exceeded, even instantaneously.

Chronic Exposure -- Exposure to a chemical for 365 days or more, as specified in the Toxicological Profiles.

Compton Effect -- An attenuation process observed for x or gamma radiation in which an incident photon interacts with an orbital electron of an atom to produce a recoil electron and a scattered photon of energy less than the incident photon.

Containment -- The confinement of radioactive material in such a way that it is prevented from being dispersed into the environment or is released only at a specified rate.

Contamination, Radioactive -- Deposition of radioactive material in any place where it is not desired, particularly where its presence may be harmful.

Cosmic Rays -- High-energy particulate and electromagnetic radiations which originate outside the earth's atmosphere.

Count (Radiation Measurements) -- The external indication of a radiation-measuring device designed to enumerate ionizing events. It may refer to a single detected event to the total number registered in a given period of time. The term often is erroneously used to designate a disintegration, ionizing event, or voltage pulse.

Counter, Geiger-Mueller -- Highly sensitive, gas-filled radiation-measuring device. It operates at voltages sufficiently high to produce avalanche ionization.

Counter, Scintillation -- The combination of phosphor, photmultiplier tube, and associated circuits for counting light emissions produced in the phosphors by ionizing radiation.

9. GLOSSARY

Curie -- A unit of activity. One curie equals 3.7x1010 nuclear transformations per second. (Abbreviated Ci.) Several fractions of the curie are in common usage.

Megacurie -- One million curies. Abbreviated MCi.

Microcurie -- One-millionth of a curie ($3.7x10^{-2}$ disintegrations per set). Abbreviated PCi.

Millicurie -- One-thousandth of a curie ($3.7x10^{7}$ disintegrations per set). Abbreviated mCi.

Nanocurie -- One-billionth of a curie. Abbreviated nCi.

Picocurie -- One-millionth of a microcurie ($3.7x10^{-2}$ disintegrations per second or 2.22 disintegrations per minute). Abbreviated pCi; replaces the term ppc.

Decay, Radioactive -- Transformation of the nucleus of an unstable nuclide by spontaneous emission of charged particles and/or photons.

Decay Chain or Decay Series -- A sequence of radioactive decays (transformations) beginning with one nucleus. The initial nucleus, the parent, decays into a daughter nucleus that differs from the first by whatever particles were emitted during the decay. If further decays take place, the subsequent nuclei are also usually called daughters. Sometimes, to distinguish the sequence, the daughter of the first daughter is called the granddaughter, etc.

Decay Constant -- The fraction of the number of atoms of a radioactive nuclide which decay in unit time. (Symbol 1). (See Disintegration Constant).

Decay Product, Daughter Product -- A new isotope formed as a result of radioactive decay. A nuclide resulting from the radioactive transformation of a radionuclide, formed either directly or as the result of successive transformations in a radioactive series. A decay product (daughter product) may be either radioactive or stable.

Delta Ray -- Energetic or swiftly moving electrons ejected from an atom during the process of ionization. Delta rays cause a track of secondary ionizations along their path.

Developmental Toxicity -- The occurrence of adverse effects on the developing organism that may result from exposure to a chemical prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism.

9. GLOSSARY

Disintegration Constant -- The fraction of the number of atoms of a radicactive nuclide which decay in unit time; λ is the symbol for the decay constant in the equation $N=N_{\circ}e^{-\lambda t}$, where $N_{\circ}$ is the initial number of atoms present, and N is the number of atoms present after same time. t. (See Decay Constant.)

Disintegration, Nuclear -- A spontaneous nuclear transformation (radioactivity) characterized by the emission of energy and/or mass from the nucleus. When large numbers of nuclei are involved, the process is characterized by a definite half-life. (See Transformation, Nuclear.)

Dose -- A general term denoting the quantity of radiation or energy absorbed. For special purposes it must be appropriately qualified. If unqualified, it refers to absorbed dose.

Absorbed Dose -- The energy imparted to matter by ionizing radiation per unit mass of irradiated material at the place of interest. The unit of absorbed dose is the rad. One rad equals 100 ergs per gram. In SI units, the absorbed dose is the gray which is 1 J/kg. (See Rad.)

Cumulative Dose (Radiation) -- The total dose resulting from repeated or continuous exposures to radiation.

Dose Assessment -- An estimate of the radiation dose to an individual or a population group usually by means of predictive modeling techniques, sometimes supplemented by the results of measurement.

Dose Equivalent (DE) -- A quantity used in radiation protection. It expresses all radiations on a common scale for calculating the effective absorbed dose. It is defined as the product of the absorbed dose in rad and certain modifying factors. (The unit of dose equivalent is the rem. In SI units, the dose equivalent is the sievert, which equals 100 rem.)

Dose, Radiation -- The amount of energy imparted to matter by ionizing radiation per unit mass of the matter, usually expressed as the unit rad, or in SI units, 100 rad-1 gray (Gy). {See Absorbed Dose.)

Maximum Permissible Dose Equivalent (MPD) -- The greatest dose equivalent that a person or specified part thereof shall be allowed to receive in a given period of time.

Median Lethal Dose (MLD) -- Dose of radiation required to kill, within a specified period, 50 percent of the individuals in a large group of animals or organisms. Also called‘the LD_{50}.

9. GLOSSARY

Threshold Dose -- The minimum absorbed dose that will produce a detectable degree of any given effect.

Tissue Dose -- Absorbed dose received by tissue in the region of interest, expressed in rad. (See Dose and Rad.)

Dose, Fractionation -- A method of administering radiation, in which relatively small doses are given daily or at longer intervals.

Dose, Protraction -- A method of administering radiation by delivering it continuously over a relatively long period at a low dose rate.

Dose-distribution Factor -- A factor which accounts for modification of the dose effectiveness in cases in which the radionuclide distribution is nonuniform.

Dose Rate -- Absorbed dose delivered per unit time.

Dosimetry -- Quantification of radiation doses to individuals or populations resulting from specified exposures.

Early Effects (of radiation exposure) -- Effects which appear within 60 days of an acute exposure.

Electron -- A stable elementary particle having an electric charge equal to $\pm 1.60210 \times 10^{-19}$g C (Coulombs) and a rest mass equal to 9.1091×10^{-31} kg. A positron is a positively charged "electron.H (See Positron.)

Electron Volt -- A unit of energy equivalent to the energy gained by an electron in passing through a potential difference of one volt. Larger multiple units of the electron volt are frequently used: keV for thousand or kilo electron volts; MeV for million or mega electron volts. (Abbreviated: eV, 1 eV-1.6×10^{-12} erg.)

Embryotoxicity and Fetotoxicity -- Any toxic effect on the conceptus as a result of prenatal exposure to a chemical; the distinguishing feature between the two terms is the stage of development during which the insult occurred. The terms, as used here, include malformations and variations, altered growth, and in utero death.

Energy -- Capacity for doing work. "Potential energy" is the energy inherent in a mass because of its spatial relation to other masses. "Kinetic energy" is the energy possessed by a mass because of its motion; MKSA unit: kg-m^2/sec^2 or joules.

Binding Energy -- The energy represented by the difference in mass between the sum of the component parts and the actual mass of the nucleus.

9. GLOSSARY

Excitation Energy -- The energy required to change a system from its ground state to an exited state. Each different excited state has a different excitation energy.

Ionizing Energy -- The average energy lost by ionizing radiation in producing an ion pair in a gas. For air, it is about 33.73 eV.

Radiant Energy -- The energy of electromagnetic radiation, such as radio waves, visible light, x and gamma rays.

Enriched Material -- (1) Material in which the relative amount of one or more isotopes of a constituent has been increased. (2) Uranium in which the abundance of the 235U isotope is increased above normal.

EPA Health Advisory -- An estimate of acceptable drinking water levels for a chemical substance based on health effects information. A health advisory is not a legally enforceable federal standard, but serves as technical guidance to assist federal, state, and local officials.

Equilibrium, Radioactive -- In a radioactive series, the state which prevails when the ratios between the activities of two or more successive members of the series remains constant.

Secular Equilibrium -- If a parent element has a very much longer half-life than the daughters (so there is not appreciable change in its amount in the time interval required for later products to attain equilibrium) then, after equilibrium is reached, equal numbers of atoms of all members of the series disintegrate in unit time. This condition is never exactly attained, but is essentially established in such a case as radium and its series to Radium D. The half-life of radium is about 1,600 years; of radon, approximately 3.82 days, and of each of the subsequent members, a few minutes. After about a month, essentially the equilibrium amount of radon is present; then (and for a long time) all members of the series disintegrate the same number of atoms per unit time.

Transient Equilibrium -- If the half-life of the parent is short enough so the quantity present decreases appreciably during the period under consideration, but is still longer than that of successive members of the series, a stage of equilibrium will be reached after which all members of the series decrease in activity exponentially with the period of the parent. An example of this is radon (half-life of approximately 3.82 days) and successive members of the series to Radium D.

Equilibrium, Radiation -- The condition in a radiation field where the energy of the radiations entering a volume equals the energy of the radiations leaving that volume.

9. GLOSSARY

Equilibrium Fraction (F) -- In radon-radon daughter equilibrium, the parents and daughters have equal radioactivity, that is, as many decay into a specific nuclide as decay out. However, if fresh radon is continually entering a volume of air or if daughters are lost by processes other than radioactive decay, e.g., plate out or migration out of the volume, a disequilibrium develops. The equilibrium fraction is a measure of the degree of equilibrium/disequilibrium. The working-level definition of radon does not take into account the amount of equilibrium. The equilibrium fraction is used to estimate working levels based on measurement of radon only.

Excitation -- The addition of energy to a system, thereby transferring it from its ground state to an excited state. Excitation of a nucleus, an atom, or a molecule can result from absorption of photons or from inelastic collisions with other particles. The excited state of an atom is a metastable state and will return to ground state by radiation of the excess energy.

Exposure -- A measure of the ionization produced in air by x or gamma radiation. It is the sum of the electrical charges on all ions of one sign produced in air when all electrons liberated by photons in a volume element of air are completely stopped in air, divided by the mass of the air in the volume element. The special unit of exposure is the roentgen.

Fission, Nuclear -- A nuclear transformation characterized by the splitting of a nucleus into at least two other nuclei and the release of a relatively large amount of energy.

Gamma Ray -- Short wavelength electromagnetic radiation of nuclear origin (range of energy from 10 keV to 9 MeV).

Genetic Effect of Radiation -- Inheritable change, chiefly mutations, produced by the absorption of ionizing radiation by germ cells. On the basis of present knowledge these effects are purely additive; there is no recovery.

Gray (Gy) -- SI unit of absorbed dose. One gray equals 100 rad. (See Units.)

Half-Life, Biological -- The time required for the body to eliminate one-half of any absorbed substance by regular processes of elimination. Approximately the same for both stable and radioactive isotopes of a particular element. This is sometimes referred to as half-time.

Half-Life, Effective -- Time required for a radioactive element in an animal body to be diminished 50% as a result of the combined action of radioactive decay and biological elimination.

9. GLOSSARY

$$\text{Effective half-life:} = \frac{\text{Biological half-life} \times \text{Radioactive half-life}}{\text{Biological half-life} + \text{Radioactive half-life}}$$

Half-life, Radioactive -- Time required for a radioactive substance to lose 50% of its activity by decay. Each radionuclide has a unique halflife.

Immediately Dangerous to Life or Health (IDLH) -- The maximum environmental concentration of a contaminant from which one could escape within 30 minutes without any escape-impairing symptoms or irreversible health effects.

Immunologic Toxicity -- The occurrence of adverse effects on the immune system that may result from exposure to environmental agents such as chemicals.

In Vitro -- Isolated from the living organism and artificially maintained, as in a test tube.

In Vivo -- Occurring within the living organism.

Intensity -- Amount of energy per unit time passing through a unit area perpendicular to the line of propagation at the point in question.

Intermediate Exposure -- Exposure to a chemical for a duration of 15 to 364 days as specified in the Toxicological Profiles.

Internal Conversion -- One of the possible mechanisms of decay from the metastable state (isomeric transition) in which the transition energy is transferred to an orbital electron, causing its ejection from the atom. The ratio of the number of internal conversion electrons to the number of gamma quanta emitted in the de-excitation of the nucleus is called the "conversion ratio."

Ion -- Atomic particle, atom, or chemical radical bearing a net electrical charge, either negative or positive.

Ion Pair -- Two particles of opposite charge, usually referring to the electron and positive atomic or molecular residue resulting after the interaction of ionizing radiation with the orbital electrons'of atoms.

Ionization -- The process by which a neutral atom or molecule acquires a positive or negative charge.

> **Primary Ionization** -- (1) In collision theory: the ionization produced by the primary particles as contrasted to the "total ionization" which includes the "secondary ionization" produced by

delta rays. (2) In counter tubes: the total ionization produced by incident radiation without gas amplification.

Specific Ionization -- Number of ion pairs per unit length of path of ionizing radiation in a medium; e.g., per centimeter of air or per micrometer of tissue,

Total Ionization -- The total electric charge of one sign on the ions produced by radiation in the process of losing its kinetic energy. For a given gas, the total ionization is closely proportional to the initial ionization and is nearly independent of the nature of the ionizing radiation. It is frequently used as a measure of radiation energy.

Ionization Density -- Number of ion pairs per unit volume.

Ionization Path (Track) -- The trail of ion pairs produced by ionizing radiation in its passage through matter.

Isobars -- Nuclides having the same mass number but different atomic numbers.

Isomers -- Nuclides having the same number of neutrons and protons but capable of existing, for a measurable time, in different quantum states with different energies and radioactive properties. Commonly the isomer of higher energy decays to one with lower energy by the process of isomeric transition.

Isotones -- Nuclides having the same number of neutrons in their nuclei.

Isotopes -- Nuclides having the same number of protons in their nuclei, and hence the same atomic number, but differing in the number of neutrons, and therefore in the mass number. Almost identical chemical properties exist between isotopes of a particular element. The term should not be used as a synonym for nuclide.

Stable Isotope -- A nonradioactive isotope of an element.

Joule -- The unit for work and energy, equal to one newton expended along a distance of one meter (lJ=lNxlm).

Labeled Compound -- A compound consisting, in part, of labeled molecules. That is molecules including radionuclides in their structure. By observations of radioactivity or isotopic composition, this compound or its fragments may be followed through physical, chemical, or biological processes.

9. GLOSSARY

Late Effects (of radiation exposure) -- Effects which appear 60 days or more following an acute exposure.

Lethal Concentration($_{LO}$)(LC_{LO}) -- The lowest concentration of a chemical in air which has been reported to have caused death in humans or animals.

Lethal Concentration($_{50}$) (LC_{50}) -- The calculated concentration of a chemical in air to which exposure for a specific length of time is expected to cause death in 50% of a defined laboratory animal population.

Lethal Dose($_{LO}$), (LD_{LO}) -- The lowest dose of a chemical introduced by a route other than inhalation that is expected to have caused death in humans or animals.

Lethal Dose($_{50}$) (LD_{50}) -- The dose of a chemical which has been calculated to cause death in 50% of a defined laboratory animal population.

Lethal Time($_{50}$) (LT_{50}) -- A calculated period of time within which a specific concentration of a chemical is expected to cause death in 50% of a defined laboratory animal population.

Linear Energy Transfer (LET) -- The average amount of energy transferred locally to the medium per unit of particle track length.

> **Low-LET --** Radiation characteristic of electrons, x-rays, and gamma rays.
>
> **High-LET --** Radiation characteristic of protons or fast neutrons.
>
> **Average LET** -- is specified to even out the effect of a particle that is slowing down near the end of its path and to allow for the fact that secondary particles from photon or fast-neutron beams are not all of the same energy.

Lowest-Observed-Adverse-Effect Level (LOAEL) -- The lowest dose of chemical in a study, or group of studies, that produces statistically or biologically significant increases in frequency or severity of adverse effects between the exposed population and its appropriate control.

Linear Hypothesis -- The assumption that a dose-effect curve derived from data in the high dose and high dose-rate ranges may be extrapolated through the low dose and low dose range to zero, implying that, theoretically, any amount of radiation will cause some damage.

9. GLOSSARY

Malformations -- Permanent structural changes in an organism that may adversely affect survival, development, or function.

Mass Numbers -- The number of nucleons (protons and neutrons) in ths nucleus of an atom. (Symbol: A)

Minimal Risk Level -- An estimate of daily human exposure to a chemical that is likely to be without an appreciable risk of deleterious effects (noncancerous) over a specified duration of exposure.

Mutagen -- A substance that causes mutations. A mutation is a change in the genetic material in a body cell. Mutation can lead to birth defects, miscarriages, or cancer.

Neurotoxicity -- The occurrence of adverse effects on the nervous system following exposure to chemical.

Neutrino -- A neutral particle of very small rest mass originally postulated to account for the continuous distribution of energy among particles in the beta-decay process.

No-Observed-Adverse-Effect Level (NOAEL) -- The dose of chemical at which there were no statistically or biologically significant increases in frequency or severity of adverse effects seen between the exposed population and its appropriate control. Effects may be produced at this dose, but they are not considered to be adverse.

Nucleon -- Common name for a constituent particle of the nucleus. Applied to a proton or neutron.

Nuclide -- A species of atom characterized by the constitution of its nucleus. The nuclear constitution is specified by the number of protons (Z) I number of neutrons (N), and energy content; or, alternatively, by the atomic number (Z), mass number A=(N+Z), and atomic mass. To be regarded as a distinct nuclide, the atom must be capable of existing for a measurable time. Thus, nuclear isomers are separate nuclides, whereas promptly decaying excited nuclear states and unstable intermediates in nuclear reactions are not so considered.

Octanol-Water Partition Coefficient (Kow) -- The equilibrium ratio of the concentrations of a chemical in n-octanol and water, in dilute solution.

Pair Production -- An absorption process for x and gamma radiation in which the incident photon is annihilated in the vicinity of the nucleus of the absorbing atom, with subsequent production of an electron and positron pair. This reaction only occurs for incident photon energies exceeding 1.02 MeV.

9. GLOSSARY

Parent -- A radionuclide which, upon disintegration, yields a specified nuclide --either directly or as a later member of a radioactive series.

Photon -- A quantity of electromagnetic energy (E) whose value ir, joules is the product of its frequency (v) in hertz and Planck constant (h). The equation is: E=hv.

Photoelectric Effect -- An attenuation process observed for x- and gamma- radiation in which an incident photon interacts with an orbital electron of an atom delivering all of its energy to produce a recoil electron, but with no scattered photon.

Positron -- Particle equal in mass to the electron (9.1091×10^{-31} kg) and having an equal but positive charge ($+1.60210 \times 10^{-19}$ Coulombs). (See Electron).

Potential Ionization -- The potential necessary to separate one electron from an atom, resulting in the formation of an ion pair.

Power, Stopping -- A measure of the effect of a substance upon the kinetic energy of a charged particle passing through it.

Progeny -- The decay products resulting after a series of radioactive decays. Progeny can also be radioactive, and the chain continues until a stable nuclide is formed.

Proton -- Elementary nuclear particle with a positive electric charge equal numerically to the charge of the electron and a rest mass of 1.007277 mass units.

q_1^* -- The upper-bound estimate of the low-dose slope of the doseresponse curve as determined by the multistage procedure. The q_1^* can be used to calculate an estimate of carcinogenic potency, the incremental excess cancer risk per unit of exposure (usually μg/L for water, mg/kg/day for food, and $\mu g/m^3$ for air).

Quality -- A term describing the distribution of the energy deposited by a particle along its track; radiations that produce different densities of ionization per unit intensity are said to have different "qualities."

Quality Factor (QF) -- The linear-energy-transfer-dependent factor by which absorbed doses are multiplied to obtain (for radiation protection purposes) a quantity that expresses - on a common scale for all ionizing radiation - the effectiveness of the absorbed dose.

Rad -- The unit of absorbed dose equal to 0.01 J/kg in any medium. (See Absorbed Dose.)

9. GLOSSARY

Radiation -- (1) The emission and propagation of energy through space or through a material medium in the form of waves; for instance, the emission and propagation of electromagnetic waves, or of sound and elastic waves. (2) The energy propagated through space or through a material medium as waves; for example, energy in the form of electromagnetic waves or of elastic waves. The term radiation or radiant energy, when unqualified, usually refers to electro-magnetic radiation. Such radiation commonly is classified, according to frequency, as Hertzian, infra-red, visible (light), ultra-violet, X-ray and gamma ray. (See Photon.) (3) By extension, corpuscular emission, such as alpha and beta radiation, or rays of mixed or unknown type, as cosmic radiation.

Annihilation Radiation -- Photons produced when an electron and a positron unite and cease to exist. The annihilation of a positron-electron pair results in the production of two photons, each of 0.51 MeV energy.

Background Radiation -- Radiation arising from radioactive material other than the one directly under consideration. Background radiation due to cosmic rays and natural radioactivity is always present. There may also be background radiation due to the presence of radioactive substances in other parts of the building, in the building material itself, etc.

Characteristic (Discrete) Radiation -- Radiation originating from an atom after removal of an electron of excitation of the nucleus. The wavelength of the emitted radiation is specific, depending only on the nuclide and particular energy levels involved.

External Radiation -- Radiation from a source outside the body -- the radiation must penetrate the skin.

Internal Radiation -- Radiation from a.source within the body (as a result of deposition of radionuclides in body tissues).

Ionizing Radiation -- Any electromagnetic or particulate radiation capable of producing ions, directly or indirectly, in its passage through matter.

Monoenergetic Radiation -- Radiation of a given type (alpha, beta, neutron, gamma, etc.) in which all particles or photons originate with and have the same energy.

Scattered Radiation -- Radiation which during its passage through a substance, has been deviated in direction. It may also have been modified by a decrease in energy.

9. GLOSSARY

Secondary Radiation -- Radiation that results from absorption of other radiation in matter. It may be either electromagnetic or particulate.

Radioactivity -- The property of certain nuclides to spontaneously emit particles or gamma radiation or x radiation following orbital electron capture or after undergoing spontaneous fission.

Artificial Radioactivity -- Man-made radioactivity produced by particle bombardment or electromagnetic irradiation, as opposed to natural radioactivity.

Induced Radioactivity -- Radioactivity produced in a substance after bombardment with neutrons or other particles. The resulting activity is "natural radioactivity" if formed by nuclear reactions occurring in nature, and "artificial radioactivity" if the reactions are caused by man.

Natural Radioactivity -- The property of radioactivity exhibited by more than 50 naturally occurring radionuclides.

Radioisotopes -- A radioactive atomic species of an element with the same atomic number and usually identical chemical properties.

Radionuclide -- A radioactive species of an atom characterized by the constitution of its nucleus.

Radiosensitivity -- Relative susceptibility of cells, tissues, organs, organisms, or any living substance to the injurious action of radiation. Radiosensitivity and its antonym, radioresistance, are currently used in a comparative sense, rather than in an absolute one.

Reaction (Nuclear) -- An induced nuclear disintegration, i.e., a process occurring when a nucleus comes in contact with a photon, an elementary particle, or another nucleus. In many cases the reaction can be represented by the symbolic equation: X+a-Y+b or, in abbreviated form, X(a,b) Y. X is the target nucleus, a is the incident particle or photon, b is an emitted particle or photon, and Y is the product nucleus.

Reference Dose (RfD) -- An estimate (with uncertainty spanning perhaps an order of magnitude) of the daily exposure of the human population to a potential hazard that is likely to be without risk of deleterious effects during a lifetime. The RfD is operationally derived from the NOAEL (from animal and human studies) by a consistent application of uncertainty factors that reflect various types of data used to estimate RfDs and an additional modifying factor, which is based on a

professional judgment of the entire database on the chemical. The RfDs are not applicable to nonthreshold effects such as cancer.

Relative Biological Effectiveness (RBE) -- The RBE is a factor used to compare the biological effectiveness of absorbed radiation doses (i.e., rad) due to different types of ionizing radiation. More specifically, it is the experimentally determined ratio of an absorbed dose of a radiation in question to the absorbed dose of a reference radiation required to produce an identical biological effect in a particular experimental organism or tissue. NOTE: This term should not be used in radiation protection. (See Quality Factor.)

Rem -- A unit of dose equivalent. The dose equivalent in rem is numerically equal to the absorbed dose in rad multiplied by the quality factor, the distribution factor, and any other necessary modifying factors.

Reportable Quantity (RQ) -- The quantity of a hazardous substance that is considered reportable under CERCLA. Reportable quantities are (1) 1 lb or greater or (2) for selected substances, an amount established by regulation either under CERCLA or under Section 311 of the Clean Water Act. Quantities are measured over a 24-hour period.

Reproductive Toxicity -- The occurrence of adverse effects on the reproductive system that may result from exposure to a chemical. The toxicity may be directed to the reproductive organs and/or the related endocrine system. The manifestation of such toxicity may be noted as alterations in sexual behavior, fertility, pregnancy outcomes, or modifications in other functions that are dependent on the integrity of this system.

Roentgen (R) -- A unit of exposure for photon radiation. One roentgen equals 2.58×10^{-4} Coulomb per kilogram of air.

Short-Term Exposure Limit (STEL) -- The maximum concentration to which workers can be exposed continually for up to 15 minutes. No more than four excursions are allowed per day, and there must be at least 60 minutes between exposure periods. The daily TLV-TWA may not be exceeded.

SI Units -- The International System of Units as defined by the General Conference of Weights and Measures in 1960. These units are generally based on the meter/kilogram/second units, with special quantities for radiation including the becquerel, gray, and sievert.

Sickness, Radiation -- (Radiation Therapy): A self-limited syndrome characterized by nausea, vomiting, diarrhea, and psychic depression following exposure to appreciable doses of ionizing radiation,

particularly to the abdominal region. Its mechanism is unknown and there is no satisfactory remedy. It usually appears a few hours after irradiation and may subside within a day. It may be sufficiently severe to necessitate interrupting the treatment series or to incapacitate the patient. (General): The syndrome associated with intense acute exposure to ionizing radiations. The rapidity with which symptoms develop is a rough measure of the level of exposure.

Sievert -- The SI unit of radiation dose equivalent. It is equal to dose in grays times a quality factor times other modifying factors, for example, a distribution factor; 1 sievert equals 100 rem.

Specific Activity -- Total activity of a given nuclide per gram of an element.

Specific Energy -- The actual energy per unit mass deposited per unit volume in a given event. This is a stochastic quantity as opposed to the average value over a large number of instance (i.e., the absorbed dose).

Standard Mortality Ratio (SMR) -- Standard mortality ratio is the ratio of the disease or accident mortality rate in a certain specific population compared with that in a standard population. The ratio is based on 200 for the standard so that an SMR of 100 means that the test population has twice the mortality from that particular cause of death.

Stopping Power -- The average rate of energy loss of a charged particle per unit thickness of a material or per unit mass of material traversed.

Surface-seeking Radionuclide -- A bone-seeking internal emitter that is deposited and remains on the surface for a long period of time. This contrasts with a volume seeker, which deposits more uniformly throughout the bone volume.

Target Organ Toxicity -- This term covers a broad range of adverse effects on target organs or physiological systems (e.g., renal, cardiovascular) extending from those arising through a single limited exposure to those assumed over a lifetime of exposure to a chemical.

Target Theory (Hit Theory) -- A theory explaining some biological effects of radiation on the basis that ionization, occurring in a discrete volume (the target) within the cell, directly causes a lesion which subsequently results in a physiological response to the damage at that location. One, two, or more "hits" (ionizing events within the target) may be necessary to elicit the response.

Teratogen -- A chemical that causes structural defects that affect the development of a fetus.

9. GLOSSARY

Threshold Limit Value (TLV) -- An allowable exposure concentration averaged over a normal 8-hour workday or 40-hour workweek.

Toxic Dose (TD_{50}) -- A calculated dose of a chemical, introduced by a route other than inhalation, which is expected to cause e specific toxic effect in 50% of a defined laboratory animal population.

Transformation, Nuclear -- The process by which a nuclide is transformed into a different nuclide by absorbing or emitting a particle.

Transition, Isomeric -- The process by which a nuclide decays to an isomeric nuclide (i.e., one of the same mass number and atomic number) of lower quantum energy. Isomeric transitions, often abbreviated I.T., proceed by gamma ray and/or internal conversion electron emission.

Tritium -- The hydrogen isotopes with one proton and two neutrons in the nucleus (Symbol: 3H or T).

Unattached Fraction -- That fraction of the radon daughters, usually ^{218}Po (Radium A), which has not yet attached to a particle. As a free atom, it has a high probability of being retained within the lung and depositing alpha energy when it decays.

Uncertainty Factor (UF) -- A factor used in operationally deriving the RfD from experimental data. UFs are intended to account for (1) the variation in sensitivity among the members of the human population, (2) the uncertainty in extrapolating animal data to the case of human, (3) the uncertainty in extrapolating from data obtained in a study that is of less than lifetime exposure, and (4) the uncertainty in using LOAEL data rather than NOAEL data. Usually each of these factors is set equal to 10.

Units, Radiological --

Units	Equivalents
Becquerel-*	1 Bq - 1 disintegration per second - 2.7×10^{-11} Ci
Curie	1 Ci - 3.7×10^{10} disintegrations per second = 3.7×10^{10} Bq
Gray*	1 GY = 1 J/kg - 100 rad
Rad	1 Rad - 100 erg/g = 0.01 Gy
Rem	1 Rem = 0.01 Sievert
Sievert*	1 sv = 100 rem

*International Units are designated (SI).

9. GLOSSARY

Working Level (WL) -- Any combination of short-lived radon daughters in 1 liter of air that will result in the ultimate emission of 1.3×10^5 MeV of potential alpha energy.

Working Level Month (WLM) -- Inhalation of air with a concentration of 1 WL of radon daughters for 170 working hours results in an exposure of 1 WLM.

X-rays -- Penetrating electromagnetic radiations whose wave lengths are shorter than those of visible light. They are usually produced by bombarding a metallic target with fast electrons in a high vacuum. In nuclear reaction, it is customary to refer to photons originating in the extranuclear part of the atom as X-rays. These rays are sometimes called roentgen rays after their discoverer, W.C. Roentgen.

APPENDIX A

PEER REVIEW

A peer review panel was assembled for plutonium. The panel consisted of the following members: Dr. Dominic Cataldo, Staff Scientist, Environmental Science Department, Battelle Northwest, Richland, Washington; Dr. Ingeborg Harding-Barlow, Consultant, Environmental and Occupationai Toxicology, Palo Alto, California; Dr. John Harley, private consultant; and Dr. Laurence Holland, Program Manager, Industrial Hygiene Group, Los Alamos National Laboratory, Los Alamos, New Mexico. These experts collectively have knowledge of radon's physical and chemical properties, toxicokinetics, key health end points, mechanisms of action, human and animal exposure, and quantification of risk to humans. All reviewers were selected in conformity with the conditions for peer review specified in Section 104(i)(13) of the Comprehensive Environmental Response, Compensation, and Liability Act of 1986, as amended.

A joint panel of scientists,from ATSDR and EPA has reviewed the peer reviewers' comments and determined which comments will be included in the profile. A listing of the peer reviewers' comments not incorporated in the profile, with a brief explanation of the rationale for their exclusion, exists as part of the administrative record for this compound. A list of databases reviewed and a list of unpublished documents cited are also included in the administrative record.

The citation of the peer review panel should not be understood to imply its approval of the profile's final content. The responsibility for the content of this profiie lies with the Agency for Toxic Substances and Disease Registry.

APPENDIX B

OVERVIEW OF BASIC RADIATION PHYSICS, CHEMISTRY AND BIOLOGY

Understanding the basic concepts in radiation physics, chemistry. and biology is important to the evaluation and interpretation of radiation-induced adverse health effects and to the derivation of radiation protection principles. This appendix presents a brief overview of the areas of radiation physics, chemistry, and biology and is based to a large extent on the reviews of Mettler and Moseley (1985), Hobbs and McClellan (1986), Eichholz (1982), Hendee (1973), and Early et al. (1979).

B.1 RADIONUCLIDES AND RADIOACTIVITY

The substances we call elements are composed of atoms. Atoms in turn are made up of neutrons, protons, and electrons; neutrons and protons in the nucleus and electrons in a cloud of orbits around the nucleus. Nuclide is the general term referring to any nucleus along with its orbital electrons. The nuclide is characterized by the composition of its nucleus and hence by the number of protons and neutrons in the. nucleus. All atoms of an element have the same number of protons (this is given by the atomic number) but may have different numbers of neutrons (this is reflected by the atomic mass or atomic weight of the element). Atoms with different atomic mass but the same atomic numbers are referred to as isotopes of an element.

The numerical combination of protons and neutrons in most nuclides is such that the atom is said to be stable; however, if there are too few or too many neutrons, the nucleus of the atom is unstable. Unstable nuclides undergo a process referred to as radioactive transformation in which energy is emitted. These unstable atoms are called radionuclides; their emissions are called ionizing radiation; and the whole property is called radioactivity. Transformation or decay results in the formation of new nuclides some of which may themselves be radionuclides, while others are stable nuclides. This series of transformations is called the decay chain of the radionuclide. The first radionuclide in the chain is called the parent; the subsequent products of the transformation are called progeny, daughters, or decay products.

In general there are two classifications of radioactivity and radionuclides: natural and man-made. Naturally-occurring radionuclides exist in nature and no additional energy is necessary to place them in an unstable state. Natural radioactivity is the property of some naturally occurring, usually heavy elements, that are heavier than lead. Radionuclides, such as radium and uranium, primarily emit alpha particles. Some lighter elements such as carbon-14 and tritium (hydrogen-3) primarily emit beta particles as they transform to a more stable atom. Natural radioactive atoms heavier than lead cannot attain

a stable nucleus heavier than lead. Everyone is exposed to background radiation from naturally-occurring radionuclides throughout life. This background radiation is the major source of radiation exposure to man and arises from several sources. The natural background exposures are frequently used as a standard of comparison for exposures to various man-made sources of ionizing radiation.

Man-made radioactive atoms are produced either as a by-product of fission of uranium atoms in a nuclear reactor or by bombarding stable atoms with particles, such as neutrons, directed at the stable atoms with high velocity. These artificially produced radioactive elements usually decay by emission of particles, such as positive or negative beta particles and one or more high energy photons (gamma rays). Unstable (radioactive) atoms of any element can be produced.

Both naturally occurring and man-made radioisotopes find application in medicine, industrial products, and consumer products. Some specific radioisotopes, called fall-out, are still found in the environment as a result of nuclear weapons use or testing.

B.2 RADIOACTIVE DECAY

B.2.1 Principles of Radioactive Decay

The stability of an atom is the result of the balance of the forces of the various components of the nucleus. An atom that is unstable (radionuclide) will release energy (decay) in various ways and transform to stable atoms or to other radioactive species called daughters, often with the release of ionizing radiation. If there are either too many or too few neutrons for a given number of protons, the resulting nucleus may undergo transformation. For some elements, a chain of daughter decay products may be produced until stable atoms are formed. Radionuclides can be characterized by the type and energy of the radiation emitted, the rate of decay, and the mode of decay. The mode of decay indicates how a parent compound undergoes transformation. Radiations considered here are primarily of nuclear origin, i.e., they arise from nuclear excitation, usually caused by the capture of charged or uncharged nucleons by a nucleus, or by the radioactive decay or transformation of an unstable nuclide. The type of radiation, may be categorized as charged or uncharged particles (electrons, neutrons, neutrinos, alpha particles, beta particles, protons, and fission products) or electromagnetic radiation (gamma rays and X-rays). Table B-l summarizes the basic characteristics of the more common types of radiation encountered.

B.2.2 Half-Life and Activity

For any given radionuclide, the rate of decay is a first-order process that depends on the number of radioactive atoms present and is

APPENDIX B

TABLE B-1. Characteristics of Nuclear Radiations

Radiation	Rest Mass	Charge	Typical Energy Range	Path Length (Order of Magnitude) Air	Path Length (Order of Magnitude) Solid	General Comments
α	4.00 amu	2+	4-10 MeV	5-10 cm	25-40 μm	Identical to ionized He nucleus
ß (negatron)	5.48×10^{-4} amu 0.51 MeV	-	0-4 MeV	0-1 m	0-1 cm	Identical to electron
Positron (ß positive)	5.48×10^{-4} amu 0.51 MeV	+	-	0-1 m	0-1 cm	Identical to electron except for charge
Proton	938.26 MeV 1.0073 amu	+	-	-	-	-
Neutron	1.0086 amu 939.55 MeV	0	0-15 MeV	0-100 m	0-100 cm	Free half life: 16 min
X (e.m. photon)	-	0	eV-100 keV	0.1-10 m[a]	0-1 m[a]	Photons from electron transitions
γ (e.m. photon)	-	0	10 KeV-3 MeV	0.1-10 m[a]	1 mm-1 m	Photons from nuclear transitions

[a]Exponential attenuation in the case of electromagnetic radiation.

α = alpha
ß = beta
X = X-ray
γ= gamma
amu = atomic mass unit
MeV = Mega electron volts
KeV = Kiloelectron volts
cm = centimeter
m = meter
μm = micrometer
mm = millimeter
e.m. = electromagnetic

characteristic for each radionuclide. The process of decay is a series of random events; temperature, pressure, or chemical combinations do not effect the rate of decay. While it may not be possible to predict exactly which atom is going to undergo transformation at any given time, it is possible to predict, on the average, how many atoms will transform during any interval of time.

The source strength is a measure of the rate of emission of radiation. For these radioactive materials it is customary to describe the source strength in terms of the source activity, which is defined as the number of disintegrations (transformations) per unit time occurring in a given quantity of this material. The unit of activity is the curie (Ci) which was originally related to the activity of one gram of radium, but is now defined as:

1 curie (Ci) = 3.7×10^{10} disintegrations (transformations)/second (dps) or
2.22×10^{12} disintegrations (transformations)/minute (dpm).

The SI unit of activity is the becquerel (Bq); 1 Bq = 1 transformation/second. Since activity is proportional to the number of atoms of the radioactive material, the quantity of any radioactive material is usually expressed incuries, regardless of its purity or concentration. The transformation of radioactive nuclei is a random process, and the rate of transformation is directly proportional to the number of radioactive atoms present. For any pure radioactive substance, the rate of decay is usually described by its radiological half-life, T_R, i.e., the time it takes for a specified source material to decay to half its initial activity.

The activity of a radionuclide at time t may be calculated by:

$$A = A_{\circ} e^{-0.693t/T} \text{rad}$$

where A is the activity in dps, A, is the activity at time zero, t is the time at which measured, and Tred is the radiological half-life of the radionuclide. It is apparent that activity exponentially decays with time. The time when the activity of a sample of radioactivity becomes one-half its original value is the radioactive half-life and is expressed in any suitable unit of time.

The specific activity is the radioactivity per unit weight of material. This activity is usually expressed in curies per gram and may be calculated by

$$\text{curies/gram} - 1.3 \times 10^{8}/(T_{rad})(\text{atomic weight})$$

where T_{rad} is the radiological half-life in days.

In the case of radioactive materials contained in living organisms, an additional consideration is made for the reduction in observed activity due to regular processes of elimination of the respective chemical or biochemical substance from the organism. This introduces a rate constant called the

biological half-life (T_{biol}) which is the time required for biological processes to eliminate one-half of the activity. This time is virtually the same for both stable and radioactive isotopes of any given element.

Under such conditions the time required for a radioactive element to be halved as a result of the combined action of radioactive decay and biological elimination is the effective half-life:

$$T_{eff} - (Tbiol \times T_{rad})/(T_{biol} + T_{rad}).$$

Table B-2 presents representative effective half-lives of particular interest.

B-2.3 Interaction of Radiation with Matter

Both ionizing and nonionizing radiation will interact with materials, that is, it will lose kinetic energy to any solid, liquid or gas through which it passes by a variety of mechanisms. The transfer of energy to a medium by either electromagnetic or particulate radiation may be sufficient to cause formation of ions. This process is called ionization. Compared to other types of radiation that may be absorbed, such as ultraviolet radiation, ionizing radiation deposits a relatively large amount of energy into a small volume.

The method by which incident radiation interacts with the medium to cause ionization may be direct or indirect. Electromagnetic radiations (X-rays and gamma photons) are indirectly ionizing; that is, they give up their energy in various interactions with cellular molecules, and the energy is then utilized to produce a fast-moving charged particle such as an electron. It is the electron that then secondarily may react with a target molecule. Charged particles, in contrast, strike the tissue or medium and directly react with target molecules, such as oxygen or water. These particulate radiations are directly ionizing radiations. Examples of directly ionizing particles include alpha and beta particles. Indirectly ionizing radiations are always more penetrating than directly ionizing particulate radiations.

Mass, charge, and velocity of a particle all affect the rate at which ionization occurs. The higher the charge of the particle and the lower the velocity, the greater the propensity to cause ionization. Heavy, highly charged particles, such as alpha particles, lose energy rapidly with distance and, therefore, do not penetrate deeply. The result of these interaction processes is a gradual slowing down of any incident particle until it is brought to rest or "stopped" at the end of its range.

B.2.4 Characteristics of Emitted Radiation

B.2.4.1 Alpha Emission. In alpha emission, an alpha particle consisting of two protons and two neutrons is emitted with a resulting decrease in the

APPENDIX B

TABLE B-2. Half-Lives of Some Radionuclides in Adult Body Organs

Radionuclide	Critical Organ	Half-Life[a]		
		Physical	Biological	Effective
Hydrogen-3[b] (Tritium)	Whole body	12.3 y	12 d	11.97d
Iodine-131	Thyroid	8 d	138 d	7.6 d
Strontium-90	Bone	28 y	50 y	18 y
Plutonium-239	Bone	24,400 y	200 y	198 y
	Lung	24,400 y	500 d	500 d
Cobalt-60	Whole body	5.3 y	99.5 d	9.5 d
Iron-55	Spleen	2.7 y	600 d	388 d
Iron-59	Spleen	45.1 d	600 d	41.9 d
Manganese-54	Liver	303 d	25 d	23 d
Cesium-137	Whole body	30 y	70 d	70 d

[a]d = days, y = years.
[b]Mixed in body water as tritiated water.

atomic mass number by four and reduction of the atomic number by two, thereby changing the parent to a different element. The alpha particle is identical to a helium nucleus consisting of two neutrons and two protons. It results from the radioactive decay of some heavy elements such as uranium, plutonium, radium, thorium, and radon. Alpha particles have a large mass as compared to electrons. Decay of alpha-emitting radionuclides may result in the emission of several different alpha particles. A radionuclide has an alpha emission with a discrete alpha energy and characteristic pattern of alpha energy emitted.

The alpha particle has an electrical charge of +2. Because of this double positive charge, alpha particles have great ionizing power, but their large size results in very little penetrating power. In fact, an alpha particle cannot penetrate a sheet of paper. The range of an alpha particle, that is, the distance the charged particle travels from the point of origin to its resting point, is about 4 cm in air, which decreases considerably to a few micrometers in tissue. These properties cause alpha emitters to be hazardous only if there is internal contamination (i.e., if the radionuclide is ingested, inhaled, or otherwise absorbed).

B.2.4.2. Beta Emission. Nuclei which are exeessively neutron rich decay by β-decay. A beta particle (β) is a high-velocity electron ejected from a disintegrating nucleus. The particle may be either a negatively charged electron, termed a negatron (β-) or a positively charged electron, termed a positron (β+). Although the precise definition of "beta emission" refers to both β- and β+, common usage of the term generally applies only to the negative particle, as distinguished from the positron emission, which refers to the β+ particle.

B.2.4.2.1 Beta Negative Emission. Beta particle (β-) emission is another process by which a radionuclide, usually those with a neutron excess, achieves stability. Beta particle emission decreases the number of neutrons by one and increases the number of protons by one, while the atomic mass remains unchanged. This transformation results in the formation of a different element. The energy spectrum of beta particle emission ranges from a certain maximum down to zero with the mean energy of the spectrum being about one-third of the maximum. The range in tissue is much less. Beta negative emitting radionuclides can cause injury to the skin and superficial body tissues but mostly present an internal contamination hazard.

B.2.4.2.2 Positron Emission. In cases in which there are too many protons in the nucleus, positron emission may occur. In this case a proton may be thought of as being converted into a neutron, and a positron (β+) is emitted, accompanied by a neutrino (see glossary). This increases the number of neutrons by one, decreases the number of protons by one, and again leaves the atomic mass unchanged. The gamma radiation resulting from the annihilation (see glossary) of the positron makes all positron emitting

isotopes more of an external radiation hazard than pure i3 emitters of equal energy.

B.2.4.2.3 Gamma Emission. Radioactive decay by alpha, beta, positron emission or electron capture often leaves some of the energy resulting from these changes in the nucleus. As a result, the nucleus is raised to an excited level. None of these excited nuclei can remain in this high-energy state. Nuclei release this energy returning to ground state or to the lowest possible stable energy level. The energy released is in the form of gamma radiation (high energy p'hotons) and has an energy equal to the change in the energy state of the nucleus. Gamma and X-rays behave similarly but differ in their origin; gamma emissions originate in the nucleus while X-rays originate in the orbital electron structure.

B.3 ESTIMATION OF ENERGY DEPOSITION IN HUMAN TISSUES

Two forms of potential radiation exposures can result -- internal and external. The term exposure denotes physical interaction of the radiation emitted from the radioactive material with cells and tissues of the human body. An exposure can be "acute" or "chronic" depending on how long an individual or organ is exposed to the radiation. Internal exposures occur when radionuclides, which have entered the body (e.g., through the inhalation, ingestion, or dermal pathways), undergo radioactive decay resulting in the deposition of energy to internal organs. External exposures occur when radiation enters the body directly from sources located outside the body, such as radiation emitters from radionuclides on ground surfaces, dissolved in water, or dispersed in the air. In general, external exposures are from material emitting gamma radiation, which readily penetrate the skin and internal organs. Beta and alpha radiation from external sources are far less penetrating and deposit their energy primarily on the skin's outer layer. Consequently, their contribution to the absorbed dose of the total body dose, compared to that deposited by gamma rays, may be negligible.

Characterizing the radiation dose to persons as a result of exposure to radiation is a complex issue. It is difficult to: (1) measure internally the amount of energy actually transferred to an organic material and to correlate any observed effects with this energy deposition; and (2) account for and predict secondary processes, such as collision effects or biologically triggered effects, that are an indirect consequence of the primary interaction event.

B.3.1 Dose Units

B.3.1.1 Roentgen. The roentgen (R) is a unit of exposure related to the amount of ionization caused in air by gamma or x-radiation. One roentgen equals 2.58×10^{-4} Coulomb per kilogram of air. In the case of gamma radiation, over the commonly encountered range of photon energy, the energy deposition in tissue for a dose of 1 R is about 0.0096 joules(J)/kg of tissue.

B.3.1.2 Absorbed Dose and Absorbed Dose Rate. Since different types of radiation interact differently with any material through which they pass, any attempt to assess their effect on humans or animals should take into account these differences. The absorbed dose is defined as the energy imparted by the incident radiation to a unit mass of the tissue or organ. The unit of absorbed dose is the rad; 1 rad - 100 erg/gram - 0.01 J/kg in any medium. The SI unit is the gray which is equivalent to 100 rad or 1 J/kg. Internal and external exposures from radiation sources are not usually instantaneous but are distributed over extended periods of time. The resulting rate of change of the absorbed dose to a small volume of mass is referred to as the absorbed dose rate in units of rad/unit time.

B.3.1.3 Working Levels and Working Level Months. Working levels are units that have been used to describe the radon decay-product activities in air in terms of potential alpha energy. It is defined as any combination of short-lived radon daughters (through polonium-214) per liter of air that will result in the emission of 1.3×10^5 MeV of alpha energy. An activity concentration of 100 pCi radon-222/L of air, in equilibrium with its daughters, corresponds approximately to a potential alpha-energy concentration of 1 WL. The WL unit can also be used for thoron daughters. In this case, 1.3×10^5 MeV of alpha energy (1 WL) is released by the thoron daughters in equilibrium with 7.5 pCi thoron/L. The potential alpha energy exposure of miners is commonly expressed in the unit Working Level Month (WLM). One WLM corresponds to exposure to a concentration of 1 WL for the reference period of 170 hours,

B.3.2 Dosimetry Models

Dosimetry models are used to estimate the internally deposited dose from exposure to radioactive substances. The models for internal dosimetry consider the quantity of radionuclides entering the body, the factors affecting their movement or transport through the body, distribution and retention of radionuclides in the body, and the energy deposited in organs and tissues from the radiation that is emitted during spontaneous decay processes. The models for external dosimetry consider only the photon doses to organs of individuals who are immersed in air or are exposed to a contaminated ground surface. The dose pattern for radioactive materials in the body may be strongly influenced by the route of entry of the material. For industrial workers, inhalation of radioactive particles with pulmonary deposition and puncture wounds with subcutaneous deposition have been the most frequent. The general population has been exposed via ingestion and inhalation of low levels of naturally occurring radionuclides as well as man-produced radionuclides from nuclear weapons testing.

B.3.2.1 Ingestion. Ingestion of radioactive materials is most likely to occur from contaminated foodstuffs or water or eventual ingestion of inhaled compounds initially deposited in the lung. Ingestion of radioactive material may result in toxic effects as a result of either absorption of the

radionuclide or irradiation of the gastrointestinal tract during passage through the tract, or a combination of both. The fraction of a radioactive material absorbed from the gastrointestinal tract is variable, depending on the specific element, the physical and chemical form of the material ingested, and the diet, as well as some other metabolic and physiological factors. The absorption of some elements is influenced by age usually with higher absorption in the very young.

B.3.2.2 Inhalation. The inhalation route of exposure has long been recognized as being of major importance for both nonradioactive and radioactive materials. The deposition of particles within the lung is largely) dependent upon the size of the particles being inhaled. After the particle is deposited, the retention will depend upon the physical and chemical properties of the dust and the physiological status of the lung. The retention of the particle in the lung depends on the location of deposition, in addition to the physical and chemical properties of the particles. The converse of pulmonary retention is pulmonary clearance. There are three distinct mechanisms of clearance which 'operate simultaneously. Ciliary clearance acts only in the upper respiratory tract. The second and third mechanisms act mainly in the deep respiratory tract. These are phagocytosis and absorption. Phagocytosis is the engulfing of foreign bodies by alveolar macrophages and their subsequent removal either up the ciliary "escalator" or by entrance into the lymphatic system. Some inhaled soluble particulates are absorbed into the blood and translocated to other organs and tissues. Dosimetric lung models are reviewed by James (1987) and James and Roy (1987).

B.3.3 Internal Emitters

The absorbed dose from internally deposited radioisotopes is the energy absorbed by the surrounding tissue. For a radioisotope distributed uniformly throughout an infinitely large medium, the concentration of absorbed energy must be equal to the concentration of energy emitted by the isotope. An infinitely large medium may be approximated by a tissue mass whose dimensions exceed the range of the particle. All alpha and most beta radiation will be absorbed in the organ (or tissue) of reference. Gamma-emitting isotope emissions are penetrating radiation and a substantial fraction may travel great distances within tissue, leaving the tissue without interacting. The dose to an organ or tissue is a function of the effective retention half-time, the energy released in the tissue, the amount of radioactivity initially introduced, and the mass of the organ or tissue.

B.4 BIOLOGICAL EFFECTS OF RADIATION

When biological material is exposed to ionizing radiation, a chain of cellular events occurs as the ionizing particle passes through the biological material. A number of theories have been proposed to describe the interaction of radiation with bioiogically important molecules in cells and to explain the resulting damage to biological systems from those interactions. Many factors

may modify the response of a living organism to a given dose of radiation. Factors related to the exposure include the dose rate, the energy of the radiation, and the temporal pattern of the exposure. Biological considerations include factors such as species, age, sex, and the portion of the body exposed. Several excellent reviews of the biological effects of radiation have been published, and the reader is referred to these for a more in-depth discussion (Hobbs and McClellan 1986; ICRP 1984; Mettler and Moseley 1985; Rubin and Casarett 1968).

B.4.1 Radiation Effects at the Cellular Level

According to Mettler and Moseley (1985), at acute doses up to 10 rad (100 mGy), single strand breaks in DNA may be produced. These single strand breaks may be repaired rapidly. With doses in the range of 50 to 500 rad (0.5 to 5 Gy) , irreparable double-stranded DNA breaks are likely, resulting in cellular reproductive death after one or more divisions of the irradiated parent cell. At large doses of radiation, usually greater than 500 rad (5 Gy), direct cell death before division (interphase death) may occur from the direct interaction of free-radicals with essentially cellular macromolecules. Morphological changes at the cellular level, the severity of which are dose-dependent, may also be observed.

The sensitivity of various cell types varies. According to the Bergonie- Tribondeau law, the sensitivity of cell lines is directly proportional to their mitotic rate and inversely proportional to the degree of differentiation (Mettler and Moseley 1985). Rubin and Casarett (1968) devised a classification system that categorized cells according to type, function, and mitotic activity. The categories range from the most sensitive type, "vegetative intermitotic cells," found in the stem cells of the bone marrow and the gastrointestinal tract, to the least sensitive cell type, "fixed postmitotic cells," found in striated muscles or long-lived neural tissues.

Cellular changes may result in cell death, which if extensive, may produce irreversible damage to an organ or tissue or may result in the death of the individual. If the cell recovers, altered metabolism and function may still occur, which may be repaired or may result in the manifestation of clinical symptoms. These changes may also be expressed at a later time as tumors or mutations.

B.4.2 Radiation Effects at the Organ Level

In most organs and tissues the injury and the underlying mechanism for that injury are complex and may involve a combination of events. The extent and severity of this tissue injury are dependent upon the radiosensitivity of the various cell types in that organ system. Rubin and Casarett (1968) describe and schematically display the events following radiation in several organ system types. These include: a rapid renewal system, such as the gastrointestinal mucosa; a slow renewal system, such as the pulmonary epithelium; and a nonrenewal system, such as neural or muscle tissue. In the

rapid renewal system, organ injury results from the direct destruction of highly radiosensitive cells, such as the stem cells in the bone marrow. Injury may also result from constriction of the microcirculation and from edema and inflammation of the basement membrane (designated as the histohematic barrier - HHB), which may progress to fibrosis. In slow renewal and nonrenewal systems, the radiation may have little effect on the parenchymal cells, but ultimate parenchymal atrophy and death over several months result from HHB fibrosis and occlusion of the micr3circulation.

B.4.3 Acute and Chronic Somatic Effects

B.4.3.1 Acute Effects. The result of acute exposure to radiation is commonly referred to as acute radiation syndrome. This effect is seen only after exposures to relatively high doses (>50 rad), which would only be expected to occur in the event of a serious nuclear accident. The four stages of acute radiation syndrome are prodrome, latent stage, manifest illness stage, recovery or death. The initial phase is characterized by nausea, vomiting, malaise and fatigue, increased temperature, and blood changes. The latent stage is similar to an incubation period. Subjective symptoms may subside, but changes may be taking place within the blood-forming organs and elsewhere which will subsequently give rise to the next stage. The manifest illness stage gives rise to symptoms specifically associated with the radiation injury. Among these symptoms are hair loss, fever, infection, hemorrhage, severe diarrhea, prostration, disorientation, and cardiovascular collapse. The symptoms and their severity depend upon the radiation dose received.

B.4.3.2 Delayed Effects. The level of exposure to radioactive pollutants that may be encountered in the environment is expected to be too low to result in the acute effects described above. When one is exposed to radiation in the environment, the amount of radiation absorbed is more likely to produce long-term effects, which manifest themselves years after the original exposure, and may be due to a single large over-exposure or continuing low-level exposure.

Sufficient evidence exists in both human populations and laboratory animals to establish that radiation can cause cancer and that the incidence of cancer increases with increasing radiation dose. Human data are extensive and include epidemiological studies of atomic bomb survivors, many types of radiation-treated patients, underground miners, and radium dial painters. Reports on the survivors of the atomic bomb explosions at Hiroshima and Nagasaki, Japan (with whole-body external radiation doses of 0 to more than 200 rad) indicate that cancer mortality has increased (Kato and Schull 1982). Use of X-rays (at doses of approximately 100 rad) in medical treatment for ankylosing spondylitis or other benign conditions or diagnostic purposes, such as breast conditions, has resulted in excess cancers in irradiated organs (BEIR 1980, 1990; UNSCEAR 1977, 1988). Cancers, such as leukemia, have been observed in children exposed <u>in utero</u> to doses of 0.2 to 20 rad (BEIR, 1980,

1990; UNSCEAR 1977, 1988). Medical use of Thorotrast (colloidal thorium dioxide) resulted in increases in the incidence of cancers of the liver, bone, and lung (ATSDR 1990a; BEIR 1980, 1990; UNSCEAR 1977, 1988). Occupational exposure to radiation provides further evidence of the ability of radiation to cause cancer. Numerous studies of underground miners exposed to radon and radon daughters, which are alpha emitters, in uranium and other hard rock mines have demonstrated increases in lung cancer in exposed workers (ATSDR 1990b). Workers who ingested radium-226 while painting watch dials had an increased incidence of leukemia and bone cancer (ATSDR 1990c). These studies indicate that depending on radiation dose and the exposure schedule, ionizing radiation can induce cancer in nearly any tissue or organ in the body. Radiation-induced cancers in humans are found to occur in the hemopoietic system, the lung, the thyroid, the liver, the bone, the skin, and other tissues.

Laboratory animal data indicate that ionizing radiation is carcinogenic and mutagenic at relatively high doses usually delivered at high dose rates. However, due to the uncertainty regarding the shape of the dose-response curve, especially at low doses, the commonly held conservative position is that the cancer may occur at dose rates that extend down to doses that could be received from environmental exposures. Estimates of cancer risk are based on the absorbed dose of radiation in an organ or tissue. The cancer risk at a particular dose is the same regardless of the source of the radiation. A comprehensive discussion of radiation-induced cancer is found in BEIR IV (1988), BEIR V (1990), and UNSCEAR (1982, 1988).

B.4.4 Genetic Effects

Radiation can induce genetic damage, such as gene mutations or chromosomal aberrations, by causing changes in the structure, number, or genetic content of chromosomes in the nucleus. The evidence for the mutagenicity of radiation is derived from studies in laboratory animals, mostly mice (BEIR 1980, 1988, 1990; UNSCBAR 1982, 1986, 1988). Evidence for genetic effects in humans is derived from tissue cultures of human lymphocytes from persons exposed to ingested or inhaled radionuclides (ATSDR 1990c, 1990d). Evidence for mutagenesis in human germ cells (cells of the ovaries or testis) is not conclusive (BEIR 1980, 1988, 1990; UNSCEAR 1977, 1986, 1988). Chromosome aberrations following radiation exposure have been demonstrated in man andn in experimental animals (BEIR 1980, 1988, 1990; UNSCEAR 1982, 1986, 1988).

B.4.5 Teratogenic Effects

There is evidence that radiation produces teratogenicity in animals. It appears that the developing fetus is more sensitive to radiation than the mother and is most sensitive to radiation-induced damage during the early stages of organ development. The type of malformation depends on the stage of development and the cells that are undergoing the most rapid differentiation at the time. Studies of mental retardation in children exposed in utero to

radiation from the atomic bomb provide evidence that radiation may produce teratogenic effects in human fetuses (Otake and Schull 19843. The damage to the child was found to be related to the dose that the fetus received.

B.5 UNITS IN RADIATION PROTECTION AND REGULATION

B.S.1 Dose Equivalent and Dose Equivalent Rate. Dose equivalent or rem is a special radiation protection quantity that is used to express the absorbed dose in a manner which considers the difference in biological effectiveness of various kinds of ionizing radiation. The ICRU has defined the dose equivalent, H, as the product of the absorbed dose, D, the quality factor, Q_1 and all other modifying factors, N, at the point of interest in biological tissue. This relationship is expressed as follows:

H –D x Q x N.

The quality factor is a dimensionless quantity that depends in part on the stopping power for charged particles, and it accounts for the differences in biological effectiveness found among the types of radiation. By definition it is independent of tissue and biological end point and, therefore, of little use in risk assessment now. Originally Relative Biolotical Effectiveness (RBE) was used rather than Q to define the quantity, rem, which was of use in risk assessment. The generally accepted values for quality factors for various radiation types are provided in Table B-3. The dose equivalent rate is the time rate of change of the dose equivalent to organs and tissues and is expressed as rem/unit time or sievert/unit time.

B.5.2 Relative Biological Effectiveness. The term relative biologic effectiveness (RBE) is used to denote the experimentally determined ratio of the absorbed dose from one radiation type to the absorbed dose of a reference radiation required to produce an identical biologic effect under the same conditions. Gamma rays from cobalt-60 and 200 to 250 KeV X-rays have been used as reference standards. The term RBE has been widely used in experimental radiobiology, and the term quality factor used in calculations of dose equivalents for radiation protection purposes (ICR? 1977; NCRP 1971; UNSCEAR 1982). The generally accepted values for RBE are provided in Table B-4.

B.S.3 Effective Dose Equivalent and Effective Dose Equivalent Rate. The absorbed dose is usually defined as the mean absorbed dose within an organ or tissue. This represents a simplification of the actual problem. Normally when an individual ingests or inhales a radionuclide or is exposed to external radiation that enters the body (gamma), the dose is not uniform throughout the whole body. The simplifying assumption is that the detriment will be the same whether the body is uniformly or nonuniformly irradiated. In an attempt to compare detriment from absorbed dose of a limited portion of the body with the detriment from total body dose, the ICRP (1977) has derived a concept of effective dose equivalent.

APPENDIX B

TABLE B-3. Quality Factors (QF)

1. X-rays, electrons, and positrons of any specific ionization

   QF = 1.

2. Heavy ionizing particles

Average LET in Water (MeV/cm)	QF
35 or less	1
35 to 70	1 to 2
70 to 230	2 to 5
230 to 530	5 to 10
530 to 1750	10 to 20

For practical purposes, a QF of 10 is often used for alpha particles[a] and fast neutrons and protons up to 10 MeV. A QF of 20 is used for heavy recoil nuclei.

[a]The ICRP (1977) recommended a quality factor of 20 for alpha particles.

LET = Linear energy transfer
MeV/cm = Megaelectron volts per centimeter
MeV = Megaelectron volts

APPENDIX B

TABLE B-4. Representative LET and RBE Values*

Radiation	Energy (MeV)	Av. LET (keV/μ)	RBE	Quality Factor
X-rays, 200 kVp	0.01-0.2	3.0	1.00	1
Gamma rays	1.25	0.3	0.7	1
	4	0.3	0.6	1
Electrons (ß)	0.1	0.42	1.0	1
	0.6	0.3	1.3	1
	1.0	0.25	1.4	--
Protons	0.1	90.0	--	6
	2.0	16.0	2	10
	5.0	8.0	2	10
Alpha particle	0.1	260.0	--	--
	5.0	95.0	10-20	10
Heavy ions	10-30	~150.0	~25	20
Neutrons	thermal		4-5	3
	1.0	20.0	2-10	10

*These values are general and approximate. RBE and QF values vary widely with different measures of biological injury.

MeV = Megaelectron volts
KeV/μ = Kiloelectron volts per micron
RBE = Relative biological effectiveness
kVp = Kilovolt potential
LET = Linear energy transfer

APPENDIX B

The effective dose equivalent, H_E, is

$$H_E = (\text{the sum of}) \; W_t \; H_t$$

where H_t is the dose equivalent in the tissue, W_t is the weighting factor, which represents the estimated proportion of the stochastic risk resulting from tissue, T, to the stochastic risk when the whole body is uniformly irradiated for occupational exposures under certain conditions (ICRP 1977). Weighting factors for selected tissues are listed in Table B-5.

The ICRU (1980), ICRP (1984), and NCRP (1985) now recommend that the rad, roentgen, curie and rem be replaced by the SI units: gray (GY), Coulomb per kilogram (C/kg), becquerel (Bq), and sievert (Sv), respectively. The relationship between the customary units and the international system of units (ST) for radiological quantities is shown in Table B-6.

APPENDIX B

TABLE B-5. Weighting Factors for Calculating Effective Dose Equivalent for Selected Tissues

Tissue	Weighting Factor
Gonads	0.25
Breast	0.15
Red bone marrow	0.12
Lung	0.12
Thyroid	0.03
Bone surface	0.03
Remainder	0.30

APPENDIX B

TABLE B-6. Comparison of Common and SI Units for Radiation Quantities

Quantity	Customary Units	Definition	SI Units	Definition
Activity (A)	Curie (Ci)	3.7×10^{10} transformations s^{-1}	becquerel (Bq)	s^{-1}
Absorbed Dose (D)		rad (rad)	$10^{-2} Jkg^{-1}$	gray (Gy) Jkg^{-1}
Absorbed Dose Rate (D)	rad per second (rad s^{-1})	$10^{-2} Jkg^{-1}s^{-1}$	gray per second (Gy s^{-1})	$Jkg^{-1}s^{-1}$
Dose Equivalent (H)	rem (rem)	$10^{-2} Jkg^{-1}$	sievert (Sv)	Jkg^{-1}
Dose Equivalent Rate (H)	rem per second (rem s^{-1})	$10^{-2} Jkg^{-1}s^{-1}$	sievert per second (Sv s^{-1})	$Jkg^{-1}s^{-1}$
Linear Energy Transfer (L_∞)	kiloelectron volts per micrometer ($keV\mu M^{-1}$)	$1.602 \times 10^{-10} Jm^{-1}$	kiloelectron volts per micrometer ($keV\mu m^{-1}$)	$1.602 \times 10^{-10} Jm^{-1}$

S^{-1} = per second
Jkg^{-1} = Joules per kilogram
$Jkg^{-1}s^{-1}$ = Joules per kilogram per second
Jm^{-1} = Joules per meter

APPENDIX B

References

ATSDR. 1990a. Toxicological profile for thorium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 1990b. Toxicological profile for radium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 199oc. Toxicological profile for radon. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

ATSDR. 1990d. Toxicological profile for uranium. U.S. Department of Health and Human Services. Public Health Service. Agency for Toxic Substances and Disease Registry. Atlanta, GA.

BEIR III. 1980. The effects on populations of exposure to low levels of ionizing radiation. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

BEIR IV. 1988. Health risks of radon and other internally deposited alpha emitters. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

BEIR V. 1990. Health effects of exposure to low levels of ionizing radiation. Committee on the Biological Effects of Ionizing Radiations, National Research Council. Washington, DC: National Academy Press.

Early P, Razzak M, Sodee D. 1979. Nuclear medicine technology. 2nd ed. St. Louis: C.V. Mosby Company.

Eichholz G. 1982. Environmental aspects of nuclear power. Ann Arbor, MI: Ann Arbor Science.

Hendee W. 1973. Radioactive isotopes in biological research. New York, NY: John Wiley and Sons.

Hobbs C, McClellan R. 1986. Radiation and radioactive materials. In: Doull J, et al., eds. Casarett and Doull's Toxicology. 3rd ed. New York, NY: Macmillan Publishing Co., Inc., 497-530.

ICRP. 1977. International Commission on Radiological Protection. Recommendations of the International Commission on Radiological Protection. ICRP Publication 26. Vol 1. No. 3. Oxford: Pergamon Press.

APPENDIX B

ICRP. 1979. International Commission on Radiological Protection. Limits for intakes of radionuclides by workers. ICRP Publication 20. Vol 3. No. 1-4. Oxford: Pergamon Press.

ICRP. 1984. International Commission on Radiological Protection. A compilation of the major concepts and quantities in use by ICRP. ICRP Publication 42. Oxford; Pergamon Press.

ICRU. 1980. International Commission on Radiation Units and Measurements. TCRU Report No. 33. Washington, DC.

James A. 1987. A reconsideration of cells at risk and other key factors in radon daughter dosimetry. In: Hopke P, ed. Radon and its decay products: Occurrence, properties and health effects. ACS Symposium Series 331. Washington, DC: American Chemical Society, 400-418.

James A, Roy M. 1987. Dosimetric lung models. In: Gerber G, et al., ed. Age-related factors in radionuclide metabolism and dosimetry. Boston: Martinus Nijhoff Publishers, 95-108.

Kato H, Schull W. 1982. Studies of the mortality of A-bomb survivors. Report 7 Part 1, Cancer mortality among atomic bomb survivors, 1950-78. Radiat Res 90:395-432.

Mettler F, Moseley R. 1985. Medical effects of ionizing radiation. New York: Grune and Stratton.

NCRP 1971. National Council on Radiation Protection and Measurements. Basic radiation protection criteria. NCRP Report No. 39. Washington, DC.

NCRP. 1985. A handbook of radioactivity measurements procedures. 2nd ed. Bethesda, MD: National Council on Radiation Protection and Measurements. NCRP Report No. 58.

Otake M, Schull W. 1984. Mental retardation in children exposed in utero to the atomic bombs: A reassessment. Technical Report RERF TR l-83, Radiation Effects Research Foundation, Japan.

Rubin P, Casarett G. 1968. Clinical radiation pathology. Philadelphia: W.B. Sanders Company, 33.

UNSCEAR. 1977. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources and effects of ionizing radiation. New York: United Nations.

UNSCEAR. 1982. United Nations Scientific Committee on the Effects of Atomic Radiation. Ionizing radiation: Sources and biological effects. New York: United Nations.

APPENDIX B

UNSCEAR. 1986. United Nations Scientific Committee on the Effects of Atomic Radiation. Genetic and somatic effects of ionizing radiation. New York: United Nations.

UNSCEAR. 1988. United Nations Scientific Committee on the Effects of Atomic Radiation. Sources, effects and risks of ionization radiation. New York: United Nations.